TROPICAL DISEASES BUREAU.

TROPICAL DISEASES BULLETIN.

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AMOEBIASIS AND DYSENTERY.

AMOEBIASIS.

SELLARDS (Andrew Watson) & THEILLER (Max). **Investigations concerning Amoebic Dysentery.**—*Amer. Jl. Trop. Med.* 1924. May. Vol. 4. No. 3. pp. 309–330. [6 refs.]

Very little information exists concerning the conditions which govern the excystment and encystment of *E. histolytica*. The generally accepted argument is that it excysts in the small intestine and that a patient cannot be re-infected with his own cysts so long as these remain in the large intestine. To test the point, specimens of faeces containing cysts of *E. histolytica*, but no trophozoites, were injected directly into the large bowel of kittens; 6 out of 8 animals became conclusively infected. Next, to eliminate the possibility of the infected animal swallowing cysts passed by itself, the large bowel was occluded at the junction of the lower and middle thirds and cysts were then injected directly into the lumen above the ligature. Three days later the bowel showed extensive deep ulceration and erosion of the mucosa and the bowel contents actively motile phagocytic entamoebae; below the ligature there were no lesions and no amoebae were found. This and other similar experiments suggest that excystation of *E. histolytica* occurs in the large bowel and is favoured by stasis. Excystation occurs under those conditions which are unfavourable for the development of trophozoites. The results of subsequent experiments indicate that a liberal supply of water is essential for successful excystation and infection. Water is absorbed so rapidly from the large intestine that the moisture of its contents is dependent upon the continued supply of fluid from the small bowel. When a ligature was placed around the middle of the colon and entamoebae were injected above and below the ligature, the bowel above the ligature was dry and free from lesions and entamoebae, while below there was an intense amoebic infection. These facts suggested that curative effects could be produced in kittens by depriving the large intestine of its supply of moisture by placing a ligature round the gut; the entamoebae disappeared promptly in the animals in which this procedure was carried out early in the course of the infection. According to this conception of the disease, the cysts of *E. histolytica* when ingested by mouth are carried rapidly by peristalsis through the small bowel and set up lesions

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at points of stasis in the large intestine, In three kittens amoebic infection rapidly invaded the ileum when the ileocolic sphincter was rendered functionless. On the other hand, ligature of the small bowel and inoculation of active amoebae immediately above the ligature failed to produce infection. This failure suggests that the environmental conditions of the ileum are unfavourable for the development of the entamoebae.

P. H. Manson-Bahr.

SMITH (S.). **Amoebiasis in Secunderabad.**—*Jl. Roy. Army Med. Corps.* 1924. May & June. Vol. 42. Nos. 5 & 6. pp. 321–330; 438–446. With 4 charts. [12 refs.]

The average admission rate for dysentery in Secunderabad during the last eight years has been 38·12 per mille, as compared with a corresponding rate of 10·18 per mille for India as a whole. In 1913 the dysentery curve for British troops showed an abrupt rise to 23·9 per mille, the average for the previous four years being 5·9 per mille. Records taken at this station during the last nine years show a definite increase of cases of amoebiasis during July and August, but the incidence of dysentery in Indian troops does not show this seasonal variation to the same degree. The "evenness" of the incidence of amoebiasis amongst various British units has been remarkable; this does not point to the spread of the infection by any individual carrier; but the corresponding seasonal incidence of simple diarrhoea and dysentery in 1923 points to some general infecting agent, *e.g.*, the house-fly, the water-supply being above suspicion. The only departure from the normal blood-picture in nine cases was a moderate eosinophilia. About one fifth of the cases were associated with colic and constipation—or "pseudo-appendicitis" group. Clinically the cases can be divided into the *acute fulminating* or *choleraic*, the acute *toxic*, the acute *non-toxic*, and the *chronic* or mild. Out of 110 cases 13·6 per cent. relapsed. Of this number 33⅓ per cent. relapsed a second time and 60 per cent. of these relapses a third. Statistics of British and Indian troops show that the former are seven times more liable to hepatic complications than the latter, while similar statistics demonstrate that though in the years 1917–1920 dysentery is almost three times more common in the southern than in the northern army, yet hepatic complications predominate in the latter. The average age incidence of 46 cases of hepatitis was found to be 27·8 years and that of liver abscess 34·7 years. The types of hepatitis may be classified into *generalized* and *acute localized*. Only two cases of liver abscess were recorded; both recovered on aspiration treatment.

P. H. M-B.

GIOSEFFI (M.). **Esiste in Italia la dissenteria amebica?**—*Riforma Med.* 1924. Feb. 11. Vol. 40. No. 6. p. 141.

Respecting the existence of amoebic dysentery in Italy before the Great War, the author calls attention to cases from Istria and Trieste seen by him in 1906 and reported in the *Gazz. degli Ospedali e delle Cliniche*, No. 12, 1910. He saw eight patients, of whom four died. The symptoms were typical and the diagnosis was confirmed by the finding of the amoeba (Charcot-Leyden crystals were found in the

stools), by the development of liver abscess in one patient, and by the post-mortem findings in the fatal cases. The bacillary variety is, however, much more frequently encountered. [See also this *Bulletin*, Vol. 21, p. 346.]

H. Harold Scott.

PETZETAKIS. **Beobachtungen ueber eine durch lebende Entamöben im Anschluss an Amöbenruhr verursachte Bronchitis. Nachweis von lebenden Entamöben im Sputum und Harn.** [Bronchitis caused by Entamoebae in Succession to Amoebic Dysentery. Demonstration of Living Entamobae in Sputum and Urine.]—*Klin. Woch.* 1924. June 3. Vol. 3. No. 23. p. 1026.

A German version of similar papers by the same worker which have already been noted in this *Bulletin*. He has recently investigated the sputum and urine in 34 cases of amoebic dysentery and has found in three (8 per cent.) living entamoebae in the sputum and in the urine in 7 (14 per cent.). The organisms in the sputum were not, he thinks, examples of *Entamoeba buccalis* as the specimens were taken after the oral cavity had been well disinfected.

P. H. M-B.

PANAYOTATOU (Angélique). **Amibiase familiale à localisations différentes. Amibiase intestinale chez la fille. Amibiase bronchique chez le père.**—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1924. Apr. 3. Year 40. Vol. 48. Ser. 3. No. 12. pp. 406–410. [1 ref.]

Inspired by her discovery of amoebic bronchitis the author reports a case occurring in a family of refugees from Asia Minor with one of amoebic dysentery in a girl of eleven years of age. The bronchitic patient, a man of forty-eight years of age, was in an enfeebled and distressed state. The viscid sputum showed a few living and numerous dead *Entamoeba histolytica* as well as cysts. Some of the organisms on a hot summer day remained alive for twenty-four hours. In size they varied from 25–35μ; the cysts, 10–14μ, contained three or four nuclei, some only two. The two cases, the author thinks, had contracted their infection from the same source, but the organism had given rise to intestinal symptoms in one case, bronchitic in the other. Both made a good recovery on emetine.

P. H. M-B.

PANAYOTATOU (Angélique). **L'amibiase des voies urinaires en Égypte.**—*Rev. Méd. et Hyg. Trop.* 1924. Apr. Vol. 16. No. 4. pp. 107–115.

The author in Alexandria has recently diagnosed and treated four cases of cystitis and two of nephritis of amoebic origin. In the urine of the cystitis cases dead and living amoebae and their cysts were passed; the nephritis cases presented the clinical picture of inflammation of the kidneys and their urine contained living and dead amoebae, but not cysts. The infection, she thinks, follows upon long standing intestinal amoebiasis, although in the case of nephritis no history of bowel infection was obtainable. The nephritis can be checked with a few doses of emetine.

The urine from one of these cases was injected into the rectum of a kitten and it developed dysentery and died on the 10th day, while another animal placed in its vicinity also succumbed with typical bowel lesions at autopsy.

P. H. M-B.

QUESADA (Fortunato). **Algunos casos de falsas apendicitis disentéricas.** —*Gac. Med. Peruana.* 1924. Jan. & Feb. Vol. 2. Nos. 13 & 14. pp. 23–27.

The author relates the main points of four cases sent into his hospital with a diagnosis of appendicitis. In all such cases examinations were made of the blood, urine and faeces. In the first patient the faeces contained ova of *Ascaris lumbricoides*, and treatment by santonin brought about a cure in four days. In the other three, *Amoeba histolytica* or its cysts were found and injections of emetine cleared up the conditions. [It is noteworthy that in no instance was there a rise of temperature or alteration of the pulse, and the highest leucocyte count was 10,000 per cmm. These facts should suffice as a warning against too hasty a diagnosis of appendicitis, the only suggested symptom in these cases being the pain and its site.]

H. Harold Scott.

MILLS (Lloyd). **Amoebic Iritis occurring in the Course of Non-Dysenteric Amoebiasis.**— *Arch. of Ophthalm.* 1923. Nov. Vol. 52. No. 6. pp. 525–545. [25 refs.]

In "toxaemic iritis" the teeth, tonsils, nasal, respiratory, genito-urinary and intestinal tracts serve in some cases as a source of septic infection. Although the etiology of the majority of these cases has now been settled by the isolation of various organisms from the eyes, there still remains a residuum usually chronic in type whose origin is obscure. In the four cases recorded in this paper bilateral iritis was associated with chronic constipation, secondary anaemia, colon tenderness and the presence of *Entamoeba histolytica* in the stools. One is related in detail. A lady of 44 had suffered from iritis for nearly 12 years, with chronic constipation, necessitating frequent enemata. In April 1921 the pain became intense, the iris being highly vascularized, while the large vessel trunks twining through the reticulum of the iris stood out like "stout vines through a trellis." The eye was enucleated and shortly after the left became similarly affected; finally an examination of the faeces revealed many "inactive Chilomastix, and a predominant number of Blastocysts and cocci" and ultimately large numbers of *Entamoeba histolytica* (whether encysted or free is not stated). Antiamoebic treatment consisted in the administration of powdered ipecacuanha in keratin-coated tablets together with $\frac{1}{3}$ gr. of emetine hydrochloride intramuscularly. Treatment continued over five months appears to have resulted in the cure of the iritis. Three other somewhat similar cases are described, in none of which was there history of diarrhoea or dysentery. The author concludes that in all cases of chronic intractable iritis of uncertain and obscure origin, especially in those patients who suffer from gastro-intestinal disorders, protozoan, and particularly amoebic infections, must be considered as a possible origin of the ocular inflammation.

[This inference requires careful consideration, quite apart from its novelty. Undoubtedly conjunctivitis and iritis are among the

recognized complications of bacillary dysentery, being due to absorption of the dysenteric toxins, and not, so far as is known, to the presence of the bacilli in the eye. The lesions of amoebiasis, on the other hand, even when extensive, are not usually accompanied by a generalized toxaemia, but are due to the activities of the specific amoebae. Dr. Mills, however, so far from producing the necessary evidence that pathogenic amoebae were present in the eyeball, states that the excised eye was not even microscopically examined. The evidence from the other three cases cannot be considered satisfactory or convincing. One is quoted on hearsay evidence as having occurred as long ago as 1912. In this case the *E. histolytica* were recorded in the stools and were banished by emetine treatment. As the patient was constipated it was probably the cysts which were observed, and at that date accurate identification of cysts was not possible, since it was not till the following year (1913) that WALKER and SELLARDS established the difference between the cysts of *E. histolytica* and *E. coli*. The author lays great stress upon the effects of antiamoebic treatment as confirmatory evidence, and we note that in the first instance emetine and ipecacuanha treatment were initiated over one year after a positive diagnosis had been made, though no exact reasons are given for the delay; in case No. 3 no appreciable improvement is recorded as having taken place.]

P. H. M-B.

FRANÇON (F.) & HUTINEL (J.). **Technique, posologie, incidents et accidents du traitement de l'amibiase hépatique par l'émétine et le novarsénobenzol.**—*L'Hôpital.* Paris. 1924. Mar. Vol. 12. No. 115. pp. 167–170. [2 refs.]

The authors believe that the best results in the treatment of amoebiasis are obtained by a combination of emetine and novarsenobillon, which for distinctiveness and convenience they designate ENV. The depressing effects of emetine are more than counterbalanced by the stimulating action of the novarsenobillon. They consider that 8 cgm. should suffice for an individual dose of emetine. The course advocated is as follows:—

Acute attack: first series, seven injections, the first two of the series 8 centigrammes each, the remainder 6 centigrammes; fifteen days' rest. Second series, seven injections of 6 centigrammes each; three weeks' interval. Third series seven injections of 5 centigrammes each.

Chronic stage: first series, six injections of 8 centigrammes each; one months' interval. Second series—five injections of 6 centigrammes, then every two months 6 centigrammes given daily for one week.

The posology for children is worked out as follows:—

	Daily dose.	Total dosage.
Under one year	0·5 cgm. ..	5 cgm.
From 1–2 years	1 ,, ..	10 ,,
From 3–5 years	2 ,, ..	20 ,,
From 5–9 years	3 ,, ..	30 ,,
From 10–13 years	4 ,, ..	40 ,,

In the method known as ENV four injections of novarsenobillon of 30 cgm. each are given at four days' interval, while on each of the three intervening days emetine is injected in gradually increasing doses from 4–8 cgm. when the emetine is suspended and the novarsenobillon injections are continued in ·3 gm. doses every four days till a total of

10 injections have been administered. After the seventh a fresh series of emetine injections in similar quantities is given.

In 40 days over 1 gramme of emetine will have been administered and 3 grammes of novarsenobillon. No serious reactions have been noted.

P. H. M-B.

BENSAUDE, CAIN & RACHET. **Les injections intraveineuses de chlorhydrate d'émétine dans le traitement de la dysenterie amibienne.**—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1924. May 15. Year 40. Vol. 48. 3rd Ser. No. 16. pp. 662–670. [1 ref.]

This is a response to the article of PETZETAKIS (see this *Bulletin*, Vol. 21, p. 342) on intravenous injections of emetine in acute intestinal amoebiasis and specially in the refractory and chronic forms of this disease. It has been shown that emetine is much less toxic when given by the intramuscular than by the intravenous route and that the drug may exert an immediate or a cumulative action; but PETZETAKIS does not appear to believe in the toxicity of the drug, although some of his patients exhibited polyneuritic symptoms.

In two cases where intravenous emetine was exhibited in the present report the initial dosage was 0·04 gm., the maximum individual dose 0·06 gm. diluted in 100 cc. and 20 cc. of normal saline respectively. One to three days elapsed between individual injections, while camphorated oil, caffeine and adrenalin were simultaneously exhibited and the patient was confined to bed. The results were by no means favourable. The second patient exhibited marked polyneuritic symptoms after 0·92 gm. of emetine, becoming inarticulate and partially paralysed.

The immediate symptoms of emetine toxaemia supervene ¼–1 hour after the injection and consist of nausea and vomiting, which may persist for the remainder of the day. Delayed toxic symptoms are due to the cumulative action of the drug and consist of asthenia, polyneuritis and cardiac involvement.

P. H. M-B.

LUDLOW (A. I.). **Treatment of Abscess of Liver by Aspiration and Subcutaneous Injections of Emetine.**—*China Med. Jl.* 1924. Feb. Vol. 38. No. 2. pp. 93–102. [6 refs.]

The subject of liver abscess has been considered by the writer in three previous papers—comprising over 100 cases. [See this *Bulletin*, Vol. 20, p. 706.] Recent experiences relating to 10 cases for the year June 1922–1923 are based entirely on the results of aspiration combined with subcutaneous injections of emetine. The protocols of the ten cases (all Koreans) are given. The comparative number of female cases (2) is higher than that recorded for other countries. The use of alcohol appeared to be a predisposing factor, and nine out of the ten gave a history of antecedent attack, or attacks, of amoebic dysentery. All abscesses occurred in the right lobe of the liver, the amount of pus on aspiration varying from 60 to 2,350 cc. The patients were infested with various other parasites—Paragonimus in two, Ancylostoma in one, Trichuris in six, and Ascaris in five. In four cases there was no appreciable leucocytosis.

In earlier years the author was not convinced that the use of emetine hastened recovery, except when amoebic dysentery was active; but probably the dosage was too small. As regards aspiration, the site of the puncture chosen was the ninth interspace in the anterior axillary

line, but, if there is a marked swelling below the costal margin or in the epigastric region, these points should be chosen. The needle should be inserted to a depth of not more than three, or, at the most, four inches. A small skin incision facilitates the introduction of the trochar. A glass (30 cc.) syringe connected with the trochar by a short, stiff rubber tube makes a simple aspirator ; if the pus be too thick 20–30 cc of Dakin's solution should be injected. All pus should be evacuated, if possible, at one aspiration ; an effusion of serum seems to take place into the cavity. Daily injections of emetine (0·06 gm.) should be continued for 6–10 doses. Should the pus prove too thick for aspiration open operation should be resorted to.

The advantages are :—Aspiration can be done under local anaesthesia, while the open method usually requires a general anaesthetic. The patient is saved the shock of an operation and the annoyance of dressings and insertion of tubes. There is less chance of secondary infection. The time in hospital is much shortened (in the ten cases it averaged 11 days). There were no deaths. Should aspiration fail, the patient is in better condition for subsequent open operation.

P. H. M-B.

Delanoë (P.). **Un cas de dysenterie amibienne grave traitée par le stovarsol.**—*Bull. Soc. Path. Exot.* 1924. Feb. 13. Vol. 17. No. 2. pp. 119–122. [3 refs.]

In a second case of amoebic dysentery stovarsol appears to have had beneficial results—a lady who seemingly had a very severe attack commencing in April, 1923. Emetine injections and permanganate lavages had little effect, but rapid amelioration took place on stovarsol (dose not stated). [The record is by no means convincing that an absolute cure had been attained.]

P. H. M-B.

Lynch (Kenneth M.). **Ingestion of Red Blood Corpuscles by an Intestinal Amoeba with Eight-Nucleated Cyst.**—*Amer. Jl. Trop. Med.* 1924. Jan. Vol. 4. No. 1. pp. 43–48. [4 refs.]

"An intestinal amoeba which is not *Endamoeba histolytica*, but which may be identified as *Endamoeba coli* by a liberal interpretation of such features as motivity, nuclear construction, thickness of cyst wall, shape of cyst, affinity for stain, and character of chromatoidal bodies, coming from a person who has had no recognizable harm from it, readily ingested red blood corpuscles in the test tube on one occasion but failed to do so on another," is the author's summary.

A. Alcock.

i. Françon (F.) & Hutinel (J.). **Les données nouvelles sur l'amibiase hépatique.**—*Bruxelles-Méd.* 1924. May 29 & June 1. Vol. 4. Nos. 51 & 52. pp. 924–933 ; 940–946. [12 refs.]

ii. Rouillard (J.). **Amibiase pulmonaire et bronchites amibiennes.**—*Presse Méd.* 1924. June 7. Vol. 32. No. 46. pp. 502–504. [8 refs.]

iii. Panayotatou (A.). **Sur quelques cas nouveaux d'amibiase extra-intestinale.**—*Bull. Soc. Path. Exot.* 1924. Mar. 12. Vol. 17. No. 3. pp. 211–214.

iv. Loiselet (J.). **Diagnostic et traitement de l'amibiase pulmonaire.**—*Rev. Prat. Malad. des Pays Chauds.* 1924. Feb. Year 2. Vol. 3. No. 6. pp. 429–446.

v. Kofoid (Charles A.) & Swezy (Olive). **A Note on Dr. Gunn's Difficulties with Councilmania.**—*Jl. Parasit.* 1924. Mar. Vol. 10. No. 3. pp. 153–157. [7 refs.]

i. Contains no original information.

ii. Contains no original observations, but is a review of recent literature on this subject.

iii. The cases recorded are two of chronic bronchitis and asthma complicated with pulmonary amoebiasis, fever and haemoptysis.

iv. A *résumé* of the previous literature of pulmonary amoebiasis as well as of the recent papers of Leclerc, Ramond, Denoyelle and Lautman, as well as of Petzetakis, all of which have been reviewed in this *Bulletin*.

P. H. M-B.

v. This is a controversial paper. It contains nothing new. The authors maintain that *Councilmania lafleuri* is a distinct species verifiable by those peculiarities of its cyst which have already been described and figured.

A. A.

BACILLARY DYSENTERY.

Megaw (J. W. D.) & Maitra (G. C.). **Chronic Dysenteric Peritonitis as the Probable Cause of a Common Form of Ascites in the Tropics.**—*Indian Med. Gaz.* 1924. May. Vol. 59. No. 5. pp. 228–232.

Ascites is a very common condition in India—at autopsy no cirrhosis of the liver is evident, but the chronic fibrosis is of the peritoneum itself. On enquiry it is found that the majority of the cases have had severe dysentery or diarrhoea shortly before. It is believed that the peritonitis is originally caused by the passage of the dysentery toxins from the bowel to the peritoneal cavity. Ascites is more likely to occur among patients who continue to be carriers of dysenteric infection: agglutinins would be more likely to persist among these carriers than among an average series of cases of recovered bacillary dysentery. In making the agglutination tests the following procedure was followed:—The bacterial emulsions were made from 18–20 hours' old agar emulsions of organisms isolated locally, the strains being kept constant, the emulsions being standardized to a definite capacity. Tubes were left in the incubator at 37°C. for two hours over a bowl of water to prevent evaporation. Readings were taken at half an hour and at room temperature. The best prospect of controlling the disease lies in the proper treatment of bacillary dysentery by salines.

The subjoined table gives a summary of the results of examinations for evidence of infection with dysentery bacilli:—

	Agglutination Response to Flexner Bacilli.					Stool Cultures for Shiga and Flexner Bacilli.		Total.
	Negative.	+1:10	+1:20	+1:40	+1:80 and over	Positive.	Negative.	
Dysenteric Ascites Group	2	0	2	2	4	2	8	10
Controls with History of Recent Dysentery	9	2	2	3	3	3	16	19
Controls giving no History of Recent Dysentery	23	7	5	4	1	0	40	40

[See also Megaw, this *Bulletin*, Vol. 19, p. 40.]

P. H. M-B.

La Favre (H. B.). **Epidemiological Report of an Outbreak of Bacillary Dysentery at the Marine Barracks Rifle Range, Santo Domingo City, Dominican Republic.**—*U.S. Nav. Med. Bull.* 1924. June. Vol. 20. No. 6. pp. 797–800.

A small epidemic of bacillary dysentery in the Marine Barracks at Santo Domingo was attended by unusual features. The disease had been endemic in Santiago for some time and the infection was imported by a small detachment of men from that city. The first case appeared four days after their arrival. There were in all 67 cases, involving 20 per cent. of the command ; only 10 were sent to hospital. The responsible organism was the Flexner bacillus. Stringent precautionary measures were taken with regard to the water supply, in which traces of faecal contamination were discovered. The author is satisfied that the outbreak is to be attributed to this source.

P. H. M-B.

Semerau (M.). **Zur Pathogenese der Ruhr.**—*Wiener Arch. f. innere Med.* Vienna. 1923. July 1. Vol. 6. pp. 395–406. [31 refs.]

It has been generally accepted that the dysenteric lesions in the intestine are due to the diffusion of the dysenteric toxin by the blood stream, but there has been no adequate explanation of the limitation of the process to the lower sections of the digestive tract. (It is generally accepted that the organisms gain entrance to the body through the mouth, though it has been shown that under normal conditions the introduction of a moderate number of dysentery bacilli into the intestinal canal does not suffice to produce an attack of " clinical " dysentery.) The diphtheritic inflammation of the rectum must probably be regarded as the result of the excretion by the mucous membrane there of bacillary toxins produced elsewhere ; the intestinal lesions thus have a twofold origin : they are due first to the entrance of the organisms into the bloodstream, and then to excretion of their toxins. Although it is generally stated that dysentery bacilli cannot be demonstrated in the bloodstream in cases of dysentery, the author does not believe this to be strictly correct, for he has collected a number of observations of Kostrzewski, who demonstrated Shiga Kruse bacilli in the blood of 28·7 per cent. of his dysentery cases.

Intravenous injections of dysentery cultures provoke in laboratory animals the characteristic necrotic changes in the mucous membrane of their intestinal canal. The failure of bacterium-free filtrates to provoke the same lesions is probably to be attributed to the absence of endotoxins in such solutions. Under normal conditions of acid secretion in the gastric juice the dysentery bacilli are rapidly destroyed on gaining entrance to the stomach. It may be that on occasions the organisms are filtered by the liver and find their way into the gall bladder, where the bile forms an efficient medium for their multiplication.

P. H. M.-B.

Robinski. **Das Syndrom der chronischen Ruhr.**—*Med. Klin.* 1924. Feb. 17. Vol. 20. No. 7. pp. 214–215. [13 refs.]

Ulcerative colitis is now generally regarded as a sequel of bacillary dysentery. It is not usually the most severe forms that become

chronic, but the typical syndrome develops after a longer or shorter latent period, with variations in individual cases. Except for occasional attacks of diarrhoea which may escape regard, the actual onset either intervenes in some other illness or takes place after severe exertion. Sleeplessness and lack of energy, tachycardia, etc., may be noted; arthritic symptoms may occur; while any dietetic error, especially the ingestion of milky or starchy foods, is liable to provoke an attack. The general appearance of the patient is one of profound cachexia. The agglutination test with dysentery bacilli may furnish a diagnosis; usually a titre of 1 : 100 against the Y bacillus is obtained; but often coagglutinins render the employment of the absorption test necessary. Demonstration of the specific organisms in these cases is very difficult.

P. H. M–B.

Hauvuy (L. E.). **Arthrite purulente du genou d'origine dysentérique bacillaire jugulée par la sérothérapie.**—*Arch. Med. et Pharm. Milit.* 1924. May. Vol. 80. No. 5. pp. 465–467.

The author records a case of acute purulent arthritis developing during the course of an acute dysentery. The knee was the joint most affected, puncture of the joint cavity yielding a purulent fluid containing an excess of polymorphonuclear leucocytes. The effusion disappeared twenty-four hours after the injection of antidysenteric serum. There were seven other cases of acute dysentery in the barracks at the time.

P. H. M–B.

Brokman (Henryk). **Badania nad wrażliwością skórną ludzi na jad czerwonkowy. Experiments on the Sensibility of the Skin of Man to the Toxin of B. Shiga-Kruse.**—*Medycyna Doświadczalna i Społeczna.* Warsaw. 1924. Vol. 2. No. 3–4. pp. 143–151. English summary p. 152.

By injecting certain doses of Shiga toxin a positive cutaneous reaction is obtained in about 80 per cent. of normal men, but it is always negative if the serum is first heated to 100° C., or neutralized *in vitro* with antitoxin. The reaction is negative in men previously injected with antitoxin, and possibly a negative reaction may coincide with immunity to dysenteric infection.

P. H. M–B.

Dutton (L. O.). **Technic for the Bacteriologic Diagnosis of Bacillary Dysentery.**—*Jl. Lab. & Clin. Med.* 1924. Apr. Vol. 9. No. 7. pp. 463–468.

Recognizing the necessity for rapid and accurate diagnosis in bacillary dysentery the author worked out a method by which positive results could be obtained, as is so desirable, in 12–15 hours. The technique, which was fully controlled, consists of plating out the faeces, or preferably mucus taken from the rectum, on to eosin-methylene-blue agar containing 0·5 per cent. each of lactose, saccharose and glycerine adjusted to pH 7·2. Suspected colonies are picked out and at least three transplanted on to Krumweide's triple sugar tubes. At the same time a mixture of several colonies is emulsified in a drop

of 1 in 30 polyvalent antidysenteric serum and mounted for slide agglutination, which should be observed over a period of one hour; a partial agglutination at the end of that time is considered as presumptive diagnosis of dysentery. The growth from the triple sugar tubes is transplanted to dextrose, maltose, mannitol and sucrose in agar with brom-cresol as the indicator, and acid formation is observed for 48–72 hours. This long period is for the purpose of giving time for the Flexner bacillus to ferment maltose, but, even then, the fermentation is always slight. The fundamental test is, however, the slide agglutination. All strains of dysentery bacilli gave complete agglutinations in dilutions of polyvalent stock antidysenteric serum as high as 1 : 50; the clumping occurring in the first five minutes.

P. H. M-B.

Boku (Shyokun). **On the Preparation of Dysentery Serum of Shiga Type for Diagnostic Purposes.**—*Chosen Igakkwai Zasshi* (*Jl. Korean Med. Assoc.* 1923. Dec. No. 45. [Summarized in *Japan Med. World.* 1924. Feb. 15. Vol. 4. No. 2. p. 37.]

The immunization of the rabbit with Shiga's bacillus offers many points of difficulty, but the author has succeeded in obtaining a high titre agglutinating serum by immunizing the rabbit with cultures heated to 100° C. The serum thus produced contained no paragglutinins to any other varieties of dysentery bacilli and thus serves well for diagnostic purposes.

P. H. M-B.

Tokuye (K.) & Hatai (K.). **The Distribution of the Dysentery Bacillus in Children affected with Dysentery.**—*Jl. Oriental Med.* Dairen. 1923. Nov. Vol. 1. No. 4. pp. 171–174.

The author describes an epidemic in Dairen. The dysentery bacillus was most frequently isolated on the first and second days of the disease. After the first week its frequency was greatly diminished. The abundance of the organism in the faeces does not always coincide with the gravity of the disease.

The Y bacillus was the most prevalent, the Flexner type was next; the original Shiga's bacillus, clinically the most severe, was relatively rare.

P. H. M-B.

Funaioli (Giulio). **Un caso di dissenteria da bacillo di Shiga in un bambino di quattro mesi.**—*Gaz. d. Ospedali e d. Cliniche.* 1924. May 4. Vol. 45. No. 18. pp. 427–428. [10 refs.]

A child, 4 months old, who had been hand-fed after the first two months, but all of whose nutriment was boiled, was attacked by diarrhoea, passing stools at first green, later, frothy, mucoid and bloodstained. Dietetic measures produced no amelioration and on examination of the stool Shiga's bacillus was isolated and the serum agglutinated this organism in a titre of 1 : 100. 10 cc. of antiserum were administered but convulsions supervened and death occurred 3 weeks after the onset of the illness. It is believed that infection was conveyed by flies settling on the teat of the bottle or on the child's lips.

H. Harold Scott.

TINNEMEYER (W.). **Zur Behandlung der Bazillenruhr.**—*Med. Klin.* 1924. Apr. 6. Vol. 20. No. 14. pp. 450–451. [2 refs.]

Owing to economic conditions the serum treatment of bacillary dysentery cannot be undertaken in Germany at present on any large scale. In the last epidemic a new form of serum treatment was given to thirty patients—a polyvalent preparation, sold under the name of "Sentocym R.D.R.P." by Kalle & Co. (Biebrich). It causes a very considerable rise in the leucocytes and is said to exert a favourable influence on the disease. No exact details are given as to the method of its preparation, but it is given in two forms—intramuscular injection and tablets to be swallowed.

In chronic bacillary dysentery the author is in favour of operative interference. It is not that the lavage of the bowel is facilitated in this manner, but the fact that the large intestine is placed entirely at rest and the faecal stream diverted from the mucous surface. With the exception of one case the results were favourable. The bowel should be rejoined after a rest of 3–5 months.

P. H. M–B.

SUZUKI (T.), with TOKUYE (K.) & HATAI (K.). **The Treatment of Dysentery with Bakteriophage.**—*Jl. Oriental Med.* Dairen. 1923. Feb. Vol. 1. No. 1. pp. 36–38.

The following experiments were made in the treatment of bacillary dysentery with bacteriophage. This substance was first isolated from the faeces of children convalescent from dysentery. It proved to be very powerful and in a dilution of one in ten million was lethal, not only to the original bacillus, but also to allied varieties. From the original bacteriophage the toxic element was removed with charcoal, leaving behind a non-toxic bacteriophage. This substance was given [? injected] into the selected 19 cases of dysentery in children, and in 46 per cent. dysentery bacilli were isolated (out of 99 examinations). In 30 untreated cases the organisms were isolated in 57·7 per cent. From these figures the authors argue that the presence of active dysentery bacilli was decreased by 11·3 per cent. Of the treated cases one died; of the untreated, six. From the clinical results obtained the authors are confident in recommending this form of treatment, for they conclude that the dysentery bacilli disappear quicker than in the non-treated cases, the agglutinating power of the blood serum is higher, and the bacteriophage is present in higher proportion than in the non-treated series.

P. H. M-B.

POZERSKI (E.). **Sur l'excrétion de composés phosphorés par les bacilles de Shiga. Modification de cette propriété lorsque les microbes ont poussé sur un milieu partiellement déshydraté.**—*C. R. Soc. Biol.* 1924. Mar. 14. Vol. 90. No. 9. pp. 602–604. [3 refs.]

Shiga's bacilli when transferred to distilled water excrete phosphorus, the amount excreted being apparently dependent upon the vitality of the organisms. When grown on dehydrated or very dry medium the organisms develop special properties. When two agar cultures, normal and dry, were taken after inoculation and incubation with the organism, in the normal tube no trace of phosphorus could be detected after the slant has been washed fifteen times, but, on the other hand,

the amount of phosphorus in the dry medium was found to be much greater. The bacilli, apparently, continue to excrete phosphorus till the organisms are no longer capable of multiplying on the medium. This property of the bacillus entirely disappears directly they are grown once more on normal agar. It is therefore dependent on the lack or presence of moisture.

P. H. M-B.

COURMONT & ROCHAIX (A.). **Variations " in vitro " de la fermentation des " sucres " par les bacilles du groupe dysentérique.**—*Jl. Physiol. et Path. Générale.* 1924. Apr. Vol. 22. No. 2. pp. 377–388. [42 refs.]

The conclusions reached are in the main comparable with those of much previous work on this subject.

By frequent subculture of the organisms on the same sugar media they come in time to acquire the power of splitting that particular carbohydrate. The four types of organism behave in different ways ; the Flexner and Hiss bacilli resemble each other in the property they acquire of fermenting sorbite, glycogen, etc. One generation of organisms can be trained to ferment a sugar to which it is unaccustomed ; this property lasts only for that generation and cannot, as a rule, be transmitted to the next ; but there are certain exceptions to this rule. Thus Shiga's bacillus can be " trained " to ferment galactose after having previously been cultured up on glucose-medium. The facts collected have demonstrated the adaptability of the dysentery bacilli, and it is probable that the modifications produced *in vitro* are more limited than those which take place in external media and especially in the intestinal canal. It therefore stands to reason that no elaborate classification of the dysentery bacilli can be based upon their fermentation reactions. One cannot rely upon biochemical reactions alone, but must apportion due share to morphology and especially to serological reactions.

P. H. M-B.

BUSSON (Bruno) & OGATA (Norio). **Untersuchungen ueber sekundäre und bakteriophagenresistente Dysenteriestämme und ihre Beziehung zu den sogenannten Schmitzstämmen.** [Secondary and Bacteriophage-resistant Strains of Dysentery Bacilli and their Relation to the so-called Schmitz Strain.]—*Wien. Klin. Woch.* 1924. July 3. Vol. 37. No. 27. pp. 665–667.

In his original work d'HERELLE stated that under the influence of his bacteriophage it was possible to produce secondary races from the original Shiga strain, differing mainly in their power of fermenting certain sugars. The authors decided to repeat these experiments, using 11 strains of Shiga, 7 of type Y, 2 Strong, 11 Flexner, 4 Schmitz and 3 bacteriophages. By injecting rabbits with a mixture of original strains which had been acted upon in a typical manner by the bacteriophage agglutinating serums were prepared. The serums thus prepared were tested against the original and secondary strains. By these means it was shown that the secondary races of organisms were no longer agglutinated by the original serum. The authors believe that the secondary races are divisible into two types ; those which permanently retain the newly acquired properties and those which do not.

The Schmitz bacilli could not be agglutinated by artificially produced immune serums. Under the influence of the bacteriophage certain Shiga bacilli acquired the property of producing indol.

P. H. M-B.

League of Nations. Health Organisation. **Reports on Serological Investigations presented to the 2nd International Conference on the Standardisation of Sera and Serological Tests held at the Pasteur Institute in Paris in November 1922.—IV. Anti-Dysentery Serum.**—pp. 78–168. [31 refs.]

Standardisation of Dysentery Serum. Report. [Doerr.] pp. 78–115.

The necessity of arriving at some international agreement on the problem of a uniform method of testing the potency of therapeutic dysentery sera is obvious.

The literature of the war contains a considerable number of reports which comment unfavourably on the results obtained by the serum treatment of bacillary dysentery. It has not been possible to form a correct judgment because the immense majority of the reports are valueless for the purposes of comparison. Excellent results have, however, been reported by so many reliable observers that it appears justifiable to conclude that this serum has a real therapeutic action, but we know very little of the conditions under which this capacity is developed to its utmost extent. The problem of standardization is by no means simple; it is not merely the determination of the amount of antitoxin, or the amount of antibody which neutralizes the Shiga-Kruse toxin, but the *method* of titration of the antitoxic components which presents difficulties. The toxins of the Shiga-Kruse bacillus are of two kinds and have two corresponding antitoxins—*anti-exotoxin* and *anti-endotoxin*. It is possible to separate the two toxins by means of elective saturation, a procedure which is equivalent to the "*heat-separation*" process.

In the pathogenesis of dysentery symptoms in man the leading part is played by the enterotropic endotoxins, but possibly the remarkably specific action of these toxins upon the organs may be susceptible of a different explanation. There is not even agreement as to whether rabbits or white mice react more regularly to the toxins of the Shiga-Kruse bacilli; or whether intraperitoneal or intravenous methods of injection should be adopted.

It must be decided whether the toxin or antitoxin is to be injected as a mixture or separately, for the results thus obtained are not comparable to those of titration of toxin-antitoxin mixtures *in vitro*.

It has been urged by Kraus that antidysenteric sera should only be allowed to be sold if 0·1 cc. injected intravenously is able to neutralize a single fatal dose of the toxin, but this is the definition of a minimum standard and there are many objections to it.

The methods of Fukuhara, based on Ehrlich's principles, are criticized, by which it appears that the dried antitoxin becomes modified into a non-toxic modification which does not possess neutralizing power; in other words, unlike the case of diphtheria toxin, the formation of *toxoids* does not take place.

The author considers the injection of serum based upon quantity rather than upon antitoxin content for clinical purposes is a source of danger, owing to the fixation of standard units without investigation

of the question as to what really should be measured. The exigencies of practice have led to the fusing of both principles of serum production and serum testing.

In titrating the toxin, experiments were carried out with rabbits and white mice—animals susceptible to the toxins. The substance was inoculated into the auricular vein of the rabbit or the caudal vein of the mouse and the following conclusions were reached :

A filtrate which is non-toxic for rabbits is equally so for white mice and *vice versa,* and there is considerable parallelism in the response of both types of animal. On the whole, the minimum lethal doses for rabbits and white mice are in the ratio of 5 : 1, but on the basis of their relative body weights, white mice have 20 times more resisting power to the Shiga toxin than rabbits. From the identity of the symptoms of poisoning in both species of animal it is evident that it is a *homogeneous toxin* which affects them both.

Whether alterations in the intestines take place in the case of rabbits after inoculation of the toxin solution depends upon factors which are governed by the condition of the animals at the time of the injection. This is the only explanation for the fact that the same dose of one and the same *toxic-filtrate* may produce serious, slight, or no changes in the intestine. After weighing up the advantages and disadvantages of the two types of laboratory animal it is urged that the use of rabbits for purposes of testing dysentery toxins and corresponding antitoxins should be maintained and white mice should not be substituted for them.

The titration value of antitoxic dysentery sera was carried out to a great extent on mice. The titration was effected by inoculation after preliminary mixing of the toxin and antitoxin *in vitro* (10–15 times the lethal dose of toxin with graduated quantities of serum, the mixture to be left standing for one hour at 37° C.). As stated above, uniform results can only be obtained if rabbits are used. Observations furnish no grounds for believing that sera which are found to be of a high therapeutic value produce better results in the treatment of dysentery patients than sera which are highly antitoxic in the ordinary sense of the word. Normal horse serum does not neutralize Shiga toxins.

Study on the Methods of Titration of Anti-Dysentery Serum. [Dopter.] pp. 116–117.

This investigator has attempted to verify the existence of endotoxins and exotoxins produced by the dysentery bacillus, but so far has failed to do so.

The best antitoxic serum was obtained from horses inoculated subcutaneously with toxin from cultures in bouillon left in the incubator at 37° C. for one week.

Investigations regarding Dysentery Toxin and Antitoxin. [Gieszczykiewicz (Marjan) & Lipinski (Witold).] pp. 118–126. [3 refs.]

The authors repeated the experiments of Olitsky and Kligler on dysentery toxins [see this *Bulletin,* Vol. 16, p. 18], but were unable fully to confirm them, notably the isolation of the neurotoxin from the enterotoxin. Simultaneously with paralysis of the extremities they

observed diarrhoea of varying intensity. Their results confirm those of DOERR to the effect that dysentery toxin is destroyed after being heated to 80° C. for three minutes.

In the case of rabbits, individual differences in the sensitiveness of the systems affected were observed; sometimes nerve symptoms, at others intestinal symptoms were more pronounced.

They therefore endeavoured to settle the question by serological methods and prepared sera which could, according to their origin, be designated antitoxic and anti-endotoxic, but experiments on animals with these sera, with living bacteria, and with extracts and toxins, revealed no qualitative differences and no special affinities with particular antigens.

Only in the agglutination test did the anti-endotoxic sera prove more potent. They concluded that for the purposes of standardization it is sufficient to determine the antitoxic properties of the serum. For the purposes of antitoxin production large doses of toxin should not be employed. Wherever possible the same breed of rabbit should be used throughout an entire series of experiments and when careful titration is adopted, cases where death occurs within twenty-four hours should be disregarded. Rabbits are preferred to mice, while 5–10 toxic doses of bouillon toxins should be employed.

Standardisation of Anti-Dysentery Serum. Interim Report transmitted by the Medical Research Council. [O'BRIEN, SUDMERSEN, EAGLETON, MACCONKEY & PETRIE.] pp. 157–159.

At the Wellcome Physiological Research Laboratories one sample of a Frankfort toxin and antitoxin were tested; the former had greatly deteriorated; the antitoxin, however, protected regularly and satisfactorily. In this case 1 mgm. of dried dysentery (Shiga) bacilli was mixed with dilutions of the serum to be tested and after half an hour was injected intravenously into a rabbit. The amount of serum necessary to neutralize the test dose of toxin was called 1 unit.

The agglutinating properties of the serum did not run parallel to the protective antibodies. If the toxin is kept hermetically sealed in phials it is found that the M.L.D. remains constant. Workers at the Lister Institute find that the toxin remains constant when stored in a desiccator in a cold room. Using pure " Shiga " toxin, sera may be obtained each cc. of which will neutralize from 1,000–6,000 M.L.D.s, but a similar titre is much more difficult to obtain when horses are immunized with *mixed* Shiga and Flexner strains.

Dysentery Serum. Report. [SHIGA (K.).] pp. 160–168.

The author describes the types of *B. dysenteriae* and directions for the manufacture of anti-dysentery serum; in the standardization of the latter mice are employed. Using the intraperitoneal method the M.L.D. is 0·1 to 0·08 mgm. for a mouse of a body weight of 12 to 14 gm.

For standardization 5 times the M.L.D. is added to a certain amount of serum. The quantity of serum which measures less than 0·0025 cc. and possesses protective power against 5 times the M.L.D. is considered effective.

P. H. M-B.

League of Nations. Health Organisation. **The Standardisation of Dysentery Serum.** First Report by Shiga (Kiyoshi), Kawamura (H.) & Tsuchiya (K.).—71 pp. With 15 charts. 1924. Geneva.

A series of experiments was carried out in order to determine a standard method of preparing a strong dysentery toxin. Toxin production is influenced by the duration of the culture ; the toxicity of the bouillon culture of the Shiga type of bacillus is highest in a two weeks' culture.

Toxin production is also influenced by the kind of peptone used in the medium ; these experiments show that Teruuchi's and fibrin peptones are somewhat superior to others, and that Chapoteaut's, as far as it could be tested, gave the best results.

Toxin production is also influenced by the reaction of the culture media ; the optimum alkalinity is pH 8·0 to 8·4 with an incubation period of from two to three weeks ; with less alkalinity the incubation period must be prolonged to obtain a given strength of toxin. When fresh grown in bouillon media the dysentery bacillus produces acid in two to three hours and the H-ion concentration increases to a maximum in six to seven hours ; at which it remains for one or two days and then decreases gradually to an alkalinity which at pH 8·6 remains steady for a long time. Unless it develops an alkalinity over pH 8·0 strong toxin cannot be obtained.

In the method of preparation of immune serum and determination of its efficiency test the most difficult point in estimating the lethal dose is the varying susceptibility of different animals. Some animals can stand three or four times the dose of others. As a whole the toxicity shows a decrease with storage. Far stronger toxin was obtained by autolysing organisms in suspension from agar culture than from bouillon culture. The use of toluol to kill the organisms yields strong toxins.

In determining the antitoxic effect of immune serum a certain amount of toxin (20 times the M.L.D. per kilogram of body weight of the rabbit) was mixed with varying amounts of the serum and incubated for half to one hour ; it was then injected intravenously to determine the amount of antitoxin which will just neutralize the toxin. Allowing for variations in the susceptibility of experimental animals and other sources of fallacy, it was found feasible to determine the maximum amount of immune serum which, when mixed with a certain amount of toxin, kills the great majority of the animals.

The amount of serum (L+) which when mixed with 20 times the M.L.D. of toxin kills the animal was taken as a unit. When the dysentery organism is used as antigen strong immunity is produced, whereas bouillon cultures or filtrates are much inferior in this respect. Sixteen horses were used for immunity work. Of six used for production of immunity with bacilli, four obtained a certain degree of immunity. The filtered toxins produced great emaciation and in three cases death. In the antitoxic tests of dysentery immune serum after exhaustive experiment it is concluded that the neutralization of dysentery toxin and antitoxin follows the law of multiplication to a certain degree, while the neutralizing value of dysentery toxin with immune serum runs parallel with the toxicity, and the method of determination of the efficacy of the immune serum with the M.L.D. of toxin gives fairly accurate results.

[This is a particularly difficult paper to summarize, as it necessarily consists of technical details, charts and protocols.]

P. H. M-B.

ZANGGER (R.). **Zur Wertbemessung der Antidysenteriesera.**—*Ztschr. f. Hyg. u. Infektionskr.* 1923. Vol. 101. No. 1. pp. 39–87. [42 refs.]

The author agrees with DOERR that in order to estimate the therapeutic value of anti-dysentery sera, it will be necessary to test monovalent sera on carefully selected human cases which have been diagnosed bacteriologically. With the knowledge so obtained one could then approach the question of a polyvalent serum. However, before this can be done it is necessary to have a reliable and standard laboratory method for the titration of anti-dysentery sera. The somewhat chaotic state in which this question is at present, as evinced by the variety of methods employed for the titration of these sera in the different serum institutes, has stimulated Zangger to investigate this question anew, in the hope of obtaining results which would pave the way to a more reliable and uniform method of titration.

Preparation and titration of dysentery toxin (*Shiga*).—The author worked with two types of toxin: (1) The filtrate from a 12 days' old broth culture; (2) a dry toxin prepared by Rowland's method (freezing and grinding bacilli with Na_2SO_4). He found these two toxins to be equally potent, giving rise to similar lesions in animals. The broth-filtrate toxin was found to be quite stable, showing little change when kept for one year under toluol in the cold (4° C.). Rabbits and mice are the best animals to employ and the intravenous route the one of choice for inoculation. The rabbit is more susceptible, and reacts more regularly to the toxin than the mouse. This difficulty, represented by the somewhat irregular reaction of animals to Shiga toxin, is well known and complicates the determination of the M.L.D. Zangger is only re-stating this difficulty when he says that the *dosis certe letalis* is more readily determined with accuracy than the *dosis letalis minima*. The principal point of interest in this section of the paper is the fact that Zangger can find no evidence in support of the division of Shiga toxin into an exotoxin (neurotoxin) and an endotoxin (enterotoxin). This conclusion of his is based on the similarity in action of the two toxins with which he worked.

Titration of Anti-sera.—Here there is little that is new. Two methods were employed: (1) Mixing the toxin and antiserum and allowing the two to act *in vitro* before inoculation; (2) inoculation of the two separately; toxin followed by anti-serum.

In both cases rabbits and white mice were employed. The author points out the necessity for fixing a definite time for the interaction of toxin and antitoxin before inoculation in method (1). Rabbits gave the most reliable results with this method, but for the sake of economy he suggests a gross titration on mice, followed by a more exact one on a small series of rabbits. For the second method the rabbit is unsuited, its susceptibility to the toxin being such that 30 *seconds* after the intravenous inoculation of 10 lethal doses of Shiga toxin, the injection of 67 times the *in vitro* neutralizing dose of serum was unable to prevent a fatal issue. The mouse, however, allows of greater latitude in this respect, it being possible to save the life of the animal even 6 hours after the injection of 10 lethal doses of toxin. Whether these two activities of the serum, neutralization *in vitro* and "curative" action *in vivo*, are due to one and the same factor (anti-toxin) the author is unable to say. This seems an important point and one which should be settled,

because unless the serum possesses some activity other than its antitoxic power, the second and more difficult method of titration is without point.

S. Phillips Bedson.

Zdansky (E.) & Herzog (B. M.). **Zur Wertbemessung der antitoxischen Dysenteriesera.**—*Ztschr. f. Hyg. u. Infektionskr.* 1924. May 28. Vol. 102. No. 3/4. pp. 352–371.

Ten batches of antidysenteric sera procured from different horses or from various specimens of venous blood from the same animal were tested; they had been prepared by various methods of producing immunity and stored for varying periods of time.

The method of titration was as follows:—

(*a*) Simultaneous equally-spaced intravenous injections into rabbits of 2½ times the lethal dose of toxin together with 0·2 to 0·4 cc. of serum.

(*b*) The intravenous injection of mixed toxin and antitoxin into white mice and rabbits.

(*c*) Intravenous injection at spaced intervals of 30 minutes of toxin and decreasing amounts of serum, white mice being employed.

The first series of experiments was conducted at the Serotherapeutic Institute in Vienna, the two last at Basle; and for this purpose a constant dose of Shiga-toxin was employed. Useful, but not always comparable, results were obtained in white mice from the toxin-antitoxin mixture.

The most exact method of estimating the potency of a serum is undoubtedly that of Zangger, which is based upon massive injections of serum into mice and subsequently into rabbits; experience having shown that a toxin mixture which is neutralized and harmless for mice is equally so for rabbits. The toxin should be a potent one and the test-dose for the mice one-tenth of that for rabbits.

P. H. M-B.

Wilkins (Lawson) & Wells (H. S.). **Immunization of Children against Flexner Dysentery.**—*Jl. Amer. Med. Assoc.* 1924. May 17. Vol. 82. No. 20. pp. 1599–1601. With 1 fig. [17 refs.]

In the summer of 1923 a vaccine was employed in an outbreak of dysentery amongst children of ages ranging from 6 months to 8 years. Dysentery had been endemic during previous summers. Prior to the general adminstration of vaccine 10 typical cases had developed, besides cases of diarrhoea which could not be classed as dysentery. The vaccine was made from organisms of the Flexner type isolated from one of the patients. The organisms were killed by heat and three doses of 250, 500 and 1,000 million given subcutaneously at intervals of three days. Of 70 children inoculated only 2 had any general reaction; most had a slight local reaction consisting of an area of redness from 1–2 cm. in diameter at the site of inoculation. There was little induration. After vaccination had been performed the disease disappeared for more than two months. In the two months following the vaccination, 18 new children were admitted directly into the institution and none of them contracted the disease.

P. H. M-B.

HULL (Thomas G.) & HENKES (Kirby). **The Agglutination of the Flexner Dysentery Bacillus by Blood Serum of Tuberculous Persons.** —*Amer. Rev. Tuberculosis.* Baltimore. 1923. Nov. Vol. 8. No. 3. pp. 272–277. [2 refs.]

The authors have already drawn attention to the agglutination of *B. dysenteriae,* Flexner—but not of other members of the typhoid-dysentery group—that occurs in patients suffering from incipient tuberculosis. The dilution of serum was made either in the ordinary manner or by dissolving a drop of blood dried on filter paper, the actual test being performed by the microscopic method. Control tests of apparently normal and healthy individuals were almost all uniformly negative. Specimens from three patients in an advanced stage of tuberculosis were negative, but in 12 cases diagnosed as definitely tuberculous 9 (75 per cent.) were positive by the agglutination test. There appears to be a substance in the blood of many individuals, including persons in the incipient stages of tuberculosis, which causes an agglutination of the Flexner bacillus.

P. H. M-B.

UNCLASSED DYSENTERY.

ANDERSON (J.). **"Dysentery: Its Diagnosis and Treatment."**— *British Guiana Med. Annual for 1923.* pp. 21–31.

The most striking feature of the Report of the Surgeon-General for British Guiana is the high rate of mortality and morbidity attributable to dysentery and allied intestinal disorders. These reports show that in 1919, 270 cases of dysentery were admitted to hospital in the big towns, with 57 deaths, while intestinal disorders in the whole colony were responsible for 1,050 deaths. The figures show that dysentery must take precedence of enteric as a serious factor in the depletion of the colony. Accuracy in the diagnosis of dysentery can never be obtained without the use of the microscope.

[The remainder of this paper is on familiar lines and is mainly based on the author's work already reviewed in this *Bulletin,* Vol. 19, p. 33.]

P. H. M-B.

FROEMSDORFF (Conrad). **Prognostische Bemerkungen ueber Ruhr.** [Remarks on Prognosis in Dysentery.]— *Arch. f. Verdauungskrankheiten.* Berlin. 1923. Dec. Vol. 32. No. 3/4. pp. 143–148. [11 refs.]

The author, impressed by the absence of reliable statistics on the prognosis of dysentery, gives figures on this subject obtained from German sources and extending over the period 1916–1920. In 1916 in a series of 12 cases the death-rate was 8·33 per cent.; in 1917 (109 cases) it was 29·35 per cent.; in 1918 (277 cases) 14·07 per cent.; in 1919 (68 cases) 8·82; and in 1920 (59 cases) 13·55 per cent. In some convalescence was very prolonged; others, after months of illness, made a permanent recovery. In the whole series of 525 cases, 415 recovered (79·04 per cent.), 22 were improved (4·19 per cent.), and 86 died (16·38 per cent.), and in 2 (0·38 per cent.) the condition remained unchanged. The death rate was high, especially so in elderly patients and in those who were greatly debilitated as a result of war privations, but the present is by no means an exceptional series, for

in the industrial districts of Westphalia the death rate from this cause stood at 10 per cent. By following up the cases over a period of six years by means of enquiries it was possible to obtain answers from 210, although 3 had died in the meantime; in no case was the death attributable to dysentery. The following statistics were obtained. In 80·95 per cent. the cure had been permanent; 6·19 per cent. had suffered from slight relapses; several suffered from digestive disturbances and irregularities of the bowel; 11·42 had suffered from diarrhoea from time to time. In 3 a definite history of *chronic* dysentery was obtained; in 1·43 per cent. of this series therefore the disease became chronic.

P. H. M-B.

Padua (Regino G.). [In English and Spanish.] **The Dysentery Problem in the Philippines. Epidemiology of a Recent Outbreak. La disenteria en Filipinas. Epidemiologia de una reciente epidemia.** —*Jl. Philippine Islands Med. Assoc.* 1924. Feb. Vol. 4. No. 2. In English, pp. 39–48. With 6 charts. [7 refs.] In Spanish, pp. 73–77.

The importance of dysentery as bearing on public health has hardly, as yet, been appreciated in the Philippines; only quite recently has an attempt been made to assign the deaths from dysentery to their respective types.

For the purpose of this paper the author has utilized all the available statistics for the last five years, which show that the death-rate from dysenteries was in that period twice that of cholera and four times that of typhoid fever—averaging 11·21 per 10,000 population in the whole archipelago. In other words, of 1,293,489 deaths from all causes during the past five years, about 57,634 were due to the dysenteries. The total death-rates from all causes have decreased in the period under review, but in Manila the mortality rates from dysentery decreased while those of typhoid increased. The death-rate from dysentery has not yet been reduced to a desired endemic limit, but the disease has become epidemic in various parts of the islands, especially during the rainy season. In Manila, when the deaths from dysentery are recorded by ages, it is found that for those under one year it is 7·06 per cent.; from 1 to 4 years, 47·74 per cent.; from 5 to 9 years, 19·51 per cent.; from 10 to 14 years, 3·14 per cent.; from 15 to 19 years, 1·76 per cent.; from 20 to 29 years, 4·63 per cent.; and 30 years and over, 16·15 per cent. The proportion of deaths from the dysenteries was relatively higher among younger children. The records frequently contain no information as to the etiology. The recent outbreak in Leyte Province was one of bacillary dysentery, although some cases of amoebic infection occurred synchronously. The spread of the infection was progressive from carriers and convalescents through polluted drinking water, flies and other insects. The prophylaxis is based upon general sanitary measures.

P. H. M-B.

Henry (T. A.) & Brown (H. C.). **Observations on Reputed Dysentery Remedies.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1923. Dec. 13 & 1924. Jan. 17. Vol. 17. Nos. 6 & 7. pp. 378–385. [17 refs.]

Amongst the drugs used as native remedies are *Monsonia ovata* and *Rhynchosia adenodes* in South Africa and *Brucea abyssinica* and *B.*

sumatrana in Abyssinia and Malaya. The authors have exhaustively examined the bark of these species without finding any well-defined active substance. The materials removed by lead acetate by precipitation from these plant extracts are rich in tannin, the effect of which was tested on Glaucoma, an actively motile free-living ciliate. Ellagic acid, acer tannin, catechin and chebulinic acid were all found to be inert, and their lack of toxicity corresponded with their lack of real tanning properties. Kurchi bark tannin and ipecacuanha tannin were found to be highly toxic. The former, *Holarrhena antidysenterica*, is well known in India as a remedy for dysentery and its value is probably due to the alkaloid, conessine, which it contains. The accumulated evidence seems to show that such action as these substances have on Glaucoma is due to the tannins themselves and not to some adhering substance. The tannins were found to belong to three classes, (*a*) the crystalline, sparingly soluble tannins which are non-toxic, (*b*) the moderately toxic tannins, typified by gallo-tannin, and (*c*) the toxic tannins, of which the best example is that derived from sant or babool pods. These three classes do not correspond with the three classes into which they may be arranged chemically. The usual decomposition products of tannins, such as gallic acid, resorcinol and catechol, are slightly toxic to Glaucoma, but certain of the higher alkyl phenols, such as *iso*-amylphenol, are markedly toxic, and this is also true of the phenolic ether constituents of some essential oils, such as nutmeg, chenopodium and anethol (from anise oil), which have been used in amoebic dysentery.

P. H. M-B.

Campos (E. de Souza). **Sur un cas de balantidiose suivie d'autopsie : colite, appendicite et lésions des ganglions lymphatiques.**—*C. R. Soc. Biol.* 1924. May 23. Vol. 90. No. 17. pp. 1341–1343.

The morbid anatomy of a fatal case of balantidiasis is here described. Small ulcerations were present in the large intestine. Histologically the necrosis extended to the upper layer of the submucosa, while the organisms were found to be numerous in the large intestine and appendix and throughout all the layers of the gut wall, not only throughout the connective tissue, but also filling the small blood vessels and lymphatics. In the necrotic areas they were found to have undergone degenerative changes. In the muscular fibres the parasites are surrounded by a clear space, while embolic masses were found embedded in the mesenteric glands.

P. H. M-B.

von Rehren (Werner). **Beitrag zur Frage der Pathogenität der *Lamblia intestinalis* bei Erkrankungen der Gallenwege und Leber.**—*Klin. Woch.* 1924. June 10. Vol. 3. No. 24. p. 1079. [13 refs.]

A short record of the discovery of *Lamblia intestinalis* in the duodenal contents of a case of jaundice in a corpulent subject of 42 years. The parasites were active and extremely numerous. The duodenum was irrigated twice weekly with 10 per cent. magnesium sulphate solution, with consequent great diminution and ultimate

disappearance of the parasites, together with the fever and jaundice. It is surmised that owing to the hypochlorhydria the parasites were able to pass through the stomach and gain a footing in the duodenum.

P. H. M-B.

KNIGHTON (J. E.). **Further Observation on the Treatment of *Lamblia Intestinalis* Infections.**—*Southern Med. Jl.* 1924. May. Vol. 17. No. 5. pp. 309–311.

The author returns to the subject of Lamblia infection with an account of four more cases, in which the history and symptoms were those of cholecystitis. *Giardia intestinalis* was very little in evidence in the faeces but was readily found in specimens of bile. Having previously tried all the usual remedies, including duodeno-biliary drainage, without lasting success, he now gave a trial to arsphenamin, and as a result he states that two or three intravenous injections of that drug (0·4 to 0·6 gm.) given at 7-day intervals will rid a patient of infection.

A. A.

HEGNER (Robert W.). **A Carnivorous Diet in the Treatment of Flagellate Diarrhea.** *Jl. Amer. Med. Assoc.* 1924. July 5. Vol. 83. No. 1. pp. 23–24. [3 refs.]

The object of this paper is to attract the attention of physicians to a reasonably argued novel method for treating intestinal troubles due to the presence of Protozoa.

Evidence exists that a carnivorous host is inauspicious to Giardia (Lamblia) and Trichomonas. Three rats, fed all their life on a carnivorous diet, were free from these flagellates, whereas their fellows fed largely on carbohydrates were abundantly infested with them; and of 15 rats fed on carnivorous diet for a week 7 per cent. lost all their Giardia and trichomonads and the other 93 per cent. lost, on an average, 90 per cent. of their Giardia and 98·2 per cent. of their trichomonads. Intestinal Protozoa, though often present in herbivorous mammals and not rare in omnivores, have very seldom been reported from carnivora; faex-examination of 12 carnivora of 10 species was negative, except in 1 case—a wild cat that had been fed on an omnivorous diet. It is suggested, therefore, that a carnivorous diet might be tried in the treatment of patients afflicted with intestinal Protozoa, or at any rate with diarrhoea due to Flagellata. A "carnivorous diet" includes fruit, toast, biscuits, butter, salad and pickles.

A. A.

DELANOË (P.). **De la fréquence des *Trichomonas* dans les selles diarrhéiques au Maroc.**—*Bull. Soc. Path. Exot.* 1924. Feb. 13. Vol. 17. No. 2. pp. 128–129. [3 refs.]

In Morocco Trichomonas must be included along with *Entamoeba histolytica* and *Balantidium coli* as a pathogenetic factor. In two cases within five months the author has found *T. intestinalis* in the stools in such numbers as to leave him in no doubt of their being the principal cause of an existing intestinal disorder.

A. A.

ANDERSON (Ch.). **Sur quelques entérites particulières présentées comme des dysenteries.**—*Bull. Soc. Path. Exot.* 1924. May 14. Vol. 17. No. 5. pp. 367–368. [1 ref.]

The author, referring to the paper of DELANOË (see p. 703), thinks that other parasites than Trichomonas are responsible for diarrhoeic conditions. Latterly he has found in such cases five instances of taeniasis, two of *Trichomonas intestinalis* and three of *Giardia intestinalis*.

P. H. M-B.

DEKESTER (M.) & MELNOTTE (P.). **Au sujet de la fréquence dans les selles diarrhéiques au Maroc des *Trichomonas* et autres protozoaires.**—*Bull. Soc. Path. Exot.* 1924. Apr. 9. Vol. 17. No. 4. pp. 301–302. [3 refs.]

In the faeces of 100 Arabs examined for intestinal flagellates the authors found Trichomonas in 6 per cent., as well as in 1·4 per cent. of hospital patients under treatment for enteritis of various kinds. They consider that *Giardia intestinalis*, *Trichomonas vaginalis* and *Tetramitus mesnili* are commensals of *Entamoeba histolytica*.

P. H. M-B.

KARKAREY (P. B.). *Ascaris lumbricoides* **and Severe Haemorrhage as Complications in a Case of Mixed Type of Dysentery.**—*Indian Med. Gaz.* 1924. Mar. Vol. 59. No. 3. pp. 141–142.

The symptoms of a severe case of mixed bacillary and amoebic dysentery were greatly relieved by the vomiting of ascaris and the passage per rectum, under santonin treatment, of a bundle of ten more. Altogether 32 were passed and the man completely recovered.

P. H. M-B.

PETRIE (A. A. W.). **The Diagnosis of Dysenteric Infections in Mental Hospitals.**—*Jl. Mental Science.* 1924. Jan. Vol. 70. No. 288. pp. 24–33. [11 refs.]

This is a well written account of dysentery compiled from a résumé of the recent literature.

P. H. M-B.

ERRATUM.

Vol. 21, No. 1, page 39, first line (CUNNINGHAM summary), for *microscopic* (examination of the stools) read *macroscopic*.

SPRUE.

ELDERS (C.). **Berust indische spruw op infectie, avitaminose of deficientie in ruimeren zin?** [Is Sprue caused by Infection, by Want of Vitamins or by Food Deficiency due to other Causes?]—*Geneesk. Gids.* 1924. Mar. 14. Vol. 1. No. 23. pp. 569–577. [4 refs.]

In a case of typical tropical sprue a bacillus was found in great quantities in the stools, resembling in all characters except one (more acid produced in cultures) UNGERMANN'S bacillus, said by BENEKE to be the cause of the disease. This facultative aërobe is closely allied to *B. acidophilus* and differs from *B. bifidus* only in the latter being an obligatory aërobe. All these species come under the head of Beijerinck's genus *Lactobacillus*, more especially under those producing laevo-lactic-acid, characterized by the metachromatic granules in their protoplasm. The bacillus was found in several other sprue patients and also in various other patients living on milk. Change from a pure milk to a mixed diet caused its disappearance. It is concluded that it has nothing to do with the aetiology of sprue and may even be considered as favourable in so far as it prevents the growth of putrefactive organisms in the intestine. No Monilia were found, because of the milk diet. ASHFORD'S (former) theory that a Monilia is the cause of sprue is rejected, though it is conceded that it may cause secondary infections in the weakened organism.

Since 1916 the author has in this way arrived at the conclusion that sprue is a deficiency disease. Further clinical experience, showing that a diet of milk and fruit, although yielding favourable results, does not prevent relapses, has brought him to prescribe a mixed diet, composed of meat (principally beefsteak), milk, oranges, strawberries, yolk of eggs, cod liver oil and limewater. Later on the juice from vegetables, still later peas and beans, are added. Carbohydrates are avoided. In a practice of almost 10 years no patient has died under this treatment.

N. H. Swellengrebel.

MANSON-BAHR (Philip). **The Morbid Anatomy and Pathology of Sprue, and their Bearing upon Aetiology.**—*Lancet.* 1924. June 7. pp. 1148–1151. With 2 figs. [16 refs.]

The author notes three points about sprue which may have a bearing on its aetiology—its reputed absence from Tropical Africa, its preference for the European, the resemblance which some cases of pernicious anaemia bear to it. The pathological appearances are not informative except in the case of autopsies on early and rapidly fatal cases; and evidence is accumulating that the essential primary lesion is ulceration of the small intestine, particularly the lower end of the ileum, either superficial or deep; in the last event death may follow from perforation. JUSTI and FISCHER and VON HECKER have published autopsies in which ulceration of the small gut was found [see this *Bulletin*, Vol. 4, p. 10; Vol. 19, p. 788].

The author describes two rapidly fatal cases and the investigations made upon them. In one, of about ten months' duration, death occurred from general peritonitis. There was found "one large ulcer

in the ileum six feet from the ileocaecal valve . . . opposite the mesenteric attachment. It measured one inch in diameter and had perforated in two places." The other case was of about the same duration and peritonitis again closed the scene.

At autopsy "the main interest centred in the ileum. The mucous membrane was acutely inflamed, with diaphanous transparent patches. Twelve ulcers of varying sizes, situated on the surface opposite the peritoneal attachment, were found, separated from each other at regular intervals of about 9 inches. The greatest number of ulcers was found in a length of gut about 4½ feet. These ulcers were more or less of the same size, roughly oval in shape, with puckered, rolled margins, and haemorrhagic bases. When held up to the light they were found to be translucent, and in all of them actual perforation of the bowel had occurred. In size they varied from 0·5 to 1 cm. The ulcers had no relation apparently to Peyer's patches, which were normal in appearance. . . . In the upper part of the jejunum one small ragged ulcer, 3 mm. in diameter and similar to those already described, was present."

Histologically there was general atrophy of the villi, a diffuse round-cell infiltration of the whole of the mucosa, general fibrosis of the submucosa, and dilatation of the capillary vessels. In the tissues underlying the ulcers were numerous granular masses of a yellowish brown pigment (haemofuscin). Lesions of the tongue, liver and spleen are described; pancreas, kidney and large intestine were healthy, or nearly so.

Discussing the pathological lesions in relation to the clinical phenomena the author notes that the bulk of the faeces may be accounted for by the large amount of non-absorbed fat in them; recent analyses suggest that this fat is already digested but fails to become absorbed through the villi owing to their destruction or to chronic inflammation evidenced by the widespread round-celled infiltration throughout the mucosa. If this view is correct, symptoms similar to those of sprue should be seen in other diseases invading the mucous membrane of the ileum, and such a case is cited in which a malignant growth of the ileum was present. The anaemia may be slight, or well marked in long-standing cases, even resembling that of pernicious anaemia. The haemolysis is, in the author's opinion, consequent upon the ulceration of the small gut, and there is evidence for this in the blood pigment within the phagocytes at the base of the ulcers, and in the ferrocyanide reaction in the liver, which was intense in the author's two cases.

No fungi were found in these cases, though cultures were made from all the organs as well as the intestine. The author regards yeasts, considered by some to be responsible for the specific lesions of sprue, as secondary invaders such as may appear in any prolonged wasting disease. He quotes McCarrison's work on monkeys, but finds no evidence that the lack of vitamins plays any part in the production of sprue, at any rate in Europeans in the East.

A. G. B.

Van Dooren (Th. P. C.). **Beschouwingen over Indische Spruw.** [Ideas concerning Tropical Sprue.]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1924. Vol. 64. No. 1. pp. 28–47. With 1 plate.

A clinical account of this disease, containing much speculation as to the etiology of sprue and few novel features. The author states that sprue is generally marked by irritation symptoms at the onset and by

symptoms of a depressive character in the later stages. Not generally known is the use of pituitrin injections against the abdominal distension caused by colonic atony.

W. J. Bais.

Hines (Laurence E.). **Studies on the Identification of** *Monilia Psilosis.* —*Jl. Infect. Dis.* 1924. May. Vol. 34. No. 5. pp. 529–535. [6 refs.]

Having recovered from the faeces of a sprue patient a yeast which exhibited the characters of *Monilia psilosis*, the author compared it with strains of fungi isolated from other stools and with other known blastomycetes. After full investigation he concluded that the morphologic and biochemical reactions of *M. psilosis* are not sufficiently distinctive to form a basis of separation from other yeasts and that common agglutinins for yeasts from various sources are readily produced in rabbits by injecting various strains of blastomycetes. Mycotic abscesses were consistently produced in animals by injecting them with old cultures of *M. psilosis*.

The evidence, as a whole, does not point to *M. psilosis* as constituting a well-defined species.

P. H. Manson-Bahr.

Rosenfeld (A. S.). [**Tropical Sprue; Necropsy.**]—*Northwest Medicine.* Seattle. 1924. Apr. Vol. 23. p. 181. [Summarized in *Jl. Amer. Med. Assoc.* 1924. May 24. Vol. 82. No. 21. p. 1732.]

Tetany occurred during the last few months of illness, when calcium lactate was given by the mouth with some relief, but later haemorrhages occurred from various orifices of the body. It is suggested that in all sprue cases therapy should be supplemented by the administration of calcium either by the mouth or intravenously.

P. H. M-B.

Bagchi (Harendra Nath). **A Case of Sprue ?**—*Calcutta Med. Jl.* 1924. Feb. Vol. 18. No. 8. pp. 619–622.

An account of a straightforward case in a native lady of Bengal, laying special stress upon the differential diagnosis of the disease.

P. H. M-B.

RABIES: A REVIEW OF RECENT ARTICLES.

The nature of the virus of rabies is a topic which has been under discussion since the time of OVID, and regarding which, as would appear from a review of the current literature, the last word has not yet been spoken. The virus is definitely infective, and in the animal host at least is capable of multiplication. In the active form in which it exists in the saliva it is a body of very small dimensions. It can pass through a porcelain bougie, and it is claimed also that it can pass through a collodion sac (LEVADITI and NICOLAU, *C. R. de l'Acad. des Sc.* 1923, Vol. 176, p. 717). It is in some manner related to the Negri body. This body according to some writers is a product of degeneration brought about by the action of the virus, and according to others is a definite phase in the life cycle of the germ of rabies. Some consider that the occurrence of Negri bodies is not absolutely specific of the presence of the germ of rabies. It is not to be wondered at that a proof of specificity resting on purely morphological grounds breaks down, but on the other hand there can be no doubt that the degree of correlation between the presence of Negri bodies on the one hand and of rabies on the other is of a very high order, and sufficient for diagnostic purposes. It is also claimed that the virus multiplies in ascitic fluid in the presence of rabbit kidney, in horse serum and citrated rabbit plasma, reproducing ultra-microscopic forms to the fourth passage. It would thus appear that the germ in a certain phase is a body of molecular dimensions, which under certain circumstances and in vitro can reproduce itself in this phase.

The criteria of "life" in its simplest form are the capacities of assimilation and of multiplication by fission. The first is essential, the second is usual but not absolutely essential. In more exact terms a system may be said to be living if it has the power of catalysing the formation of systems similar in constitution to itself from more elementary compounds. In this connexion one is reminded of Brailsford ROBERTSON's theory of growth as a process of autocatalysis. If the dimensions of the living individual are of so small an order that it is able to pass through a collodion sac, that is to say, if the living unit is smaller than an albumen molecule, but larger than a molecule of peptone, or of an amino acid, one is led into interesting speculations.

Let us in the first place follow the recent work of those who believed the germ to be a protozoon of the type of the microsporidia.

LEVADITI (1, 2, 3, 4) and his co-workers describe a life cycle in which the Negri body takes its place as a pansporoblast, which is formed only in neurones which are physiologically and morphologically healthy. Where degeneration has occurred no pansporoblasts are found. The pansporoblasts contain "plages," each of which is an aggregate of microsporidium spores, and round them the neurone of the host secretes a hyaline substance which forms a capsule, isolating the colony from

1–4. LEVADITI (C.), NICOLAU (S.) & SCHOEN (R.). La microsporidiose du lapin ; ses relations avec la rage.—*C.R. Acad. Sci.* 1924. Jan. 7. Vol. 178. No. 2. pp. 256–258. [4 refs.] ; La nature microsporidienne du virus rabique. —*C.R. Soc. Biol.* 1924. Feb. 22. Vol. 90. No. 6. pp. 398–402. [4 refs.] ; La nature du virus rabique.—*Ibid.* Apr. 18. Vol. 90. No. 14. pp. 994–997. [1 ref.] ; La nature du virus rabique fixe.—*Ibid.* June 20. Vol. 91. No. 21. pp. 56–58. [1 ref.]

the rest of the cell. This pansporoblastic phase appears in the affected animal before symptoms have appeared, the clinical signs of the disease being ascribed to the action of the discrete germ. They consider also that the germ behaves differently in different regions, the pansporoblastic stage depending upon not only the physiological integrity of the neurone, but also upon its embryological character, and further, that the absence of the Negri bodies in fixed virus rabies may be accounted for by the fact that the rate of multiplication of ultramicroscopic forms is so rapid that the animal dies before cystic forms have developed. They suggest that the parasite be called *Glugea lyssa*.

An attempt to revert to the formation of Negri bodies by successively subpassaging fixed virus through the brains of three monkeys (the last of which was a chimpanzee) failed. The authors note that the virulence of this virus, which had been fixed by intracranial subpassage through rabbits, was retained, the chimpanzee dying after an incubation period of eight days. They seem to have overlooked the fact that rabies virus can be fixed in the rabbit, or the dog, or the monkey (macacus), provided that it is introduced intracerebrally. Fixed virus is no doubt a mutation of street virus, but the mutation is not occasioned by the species of the animal concerned so much as by the nature of the tissue upon which it is implanted.

Manouelian and Viala (5, 6) describe the active phase as consisting of elongated fusiform or piriform bodies averaging 1 to 2μ in length, but frequently smaller, and just at the limit of visibility. These they claim are found in all forms of rabies and in all virulent organs. They are found in the salivary glands, and stain similarly to protozoa. They are always intracellular. They consider that Negri body formation is due to the degeneration of these intracellular forms, and is brought about by their agglutination into masses which ultimately coalesce. Manouelian applies the name *Encephalitozoon rabiei* to these bodies.

Vomela (7) summarizes the views of those who hold that Negri bodies are reaction-products of the nerve cells against the virus. The total absence of Negri bodies in certain cases of rabies; their presence in some parts and absence from other parts of the nervous system though each are definitely infective; the proved ultramicroscopic nature of the virus; and the fact that the size of the body depends largely upon the size of the animal affected, have led him to this conclusion.

It is quite obvious that from all this nothing has been proved. Morphological methods must break down when applied to structures which are beyond or just bordering upon the limit of visibility. This applies to the upholders of either view, for even as it is impossible to prove the existence of structure under these conditions, so also is it impossible to make a definite statement to the contrary.

Attention has been directed by Remlinger to variations of virulence of fixed virus as a result of long continued subpassage. The original strain of fixed virus is now in about its 2,000th passage. Remlinger

5, 6. Manouelian (Y.) & Viala (J.). *Encephalitozoon rabiei* parasite de la rage. —*C.R. Acad. Sci.* 1924. Jan. 14. Vol. 178. No. 3. pp. 344–345. [1 ref.]; *Ann. Inst. Pasteur.* 1924. Mar. Vol. 38. No. 3. pp. 258–267 With 4 plates. [9 refs.]

7. Vomela (Stanislav). Das Centralnervensystem bei der Lyssa.—*Bibliothèqu Microbiol. Tchéco-Slovaque.* 1923. T. 4. 18 pp. [19 refs.]

(8, 9, 10, 11) claims that marked changes have occurred in its properties. It has become inoffensive to man, and it has also become less resistant to desiccation and to the action of glycerine. He is of opinion that a cord which has been dried for 3–4 days at the 2,000th passage corresponds to one which was dried 6–7 days in early Pasteurian times. Le Fèvre de Arric and Tchang Kouo-Ngen (12) criticize these generalizations. They compare the strain in use in Brussels, which emanated from Paris ten years previously, with the strain at present employed in Paris, and between these they demonstrate considerable differences. The Brussels strain is in general the more virulent. They rightly conclude that the differences which are observed depend upon the treatment which the virus has received in the different institutes. This is well known to rabies workers, and is a statistical necessity. It has been shown, for example, that continued selection for subpassage of brains of animals which have died of rabies with incubation periods of less than average duration tends to shorten the incubation period of the strain.

In connexion with the experiments cited above Remlinger proposes the use of glycerine attenuation in place of desiccation in the preparation of material for antirabic inoculation. He points out that when brain material is placed in glycerine the loss of virulence proceeds centripetally, and that consequently the virus remains alive for a longer period of time in those portions of brain which have the greatest radius. Thus the effect of glycerine is very similar to that of desiccation, for it was pointed out by Harvey and McKendrick that in cords which are dried in an exsiccator the process also proceeds centripetally, the loss of virulence agreeing almost exactly with the loss of weight resulting from the abstraction of water. The use of the term attenuation in this sense is somewhat unfortunate. The process is analogous to that of disinfection, and it has still to be shown that those organisms which survive the action of disinfectants over unusually long periods of time (*vide* the work of Harriette Chick) have been modified by the disinfectant. The phenomenon proceeds according to the law of mass action, that is to say it depends upon the chances of occurrence of collisions. The conception of attenuation depends upon our definition of virulence—and the virulence of invisible filtrable virus depends upon such unknown factors as its concentration, its rate of multiplication, and finally upon the specific aggressiveness of the individual germ. Rodet (13) and Rochaix (14) follow Remlinger

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8–11. Remlinger (P.). Contribution à l'étude de l'action de la glycérine sur le virus rabique.—*C.R. Soc. Biol.* 1924. Jan. 25. Vol. 90. No. 2. pp. 70–72; Une nouvelle méthode de traitement antirabique. Les moelles glycérinées fraîches.—*Ibid.* 1924. Feb. 8. Vol. 90. No. 4. pp. 272–273; Sur quelques modifications susceptibles d'être apportées au traitement antirabique.—*Bull. Acad. Med.* 1924. Feb. 5. Year 88. 3rd Ser. Vol. 91. No. 6. pp. 199–204. [6 refs.]; *Arch. Inst. Pasteur de Tunis.* 1924. Apr. Vol. 13. No. 1. pp. 114–119. [6 refs.]

12. Le Févre de Arric (M.) & Tchang Kouo-Ngen (J.). Activité comparée du virus rabique fixe entretenu à Paris et à Bruxelles.—*C.R. Soc. Biol.* 1924. Apr. 11. Vol. 90. No. 13. pp. 980–982. [5 refs.]

13. Rodet (A.). A propos de l'action de la glycérine sur le virus rabique.—*C.R. Soc. Biol.* 1924. May 16. Vol. 90. No. 16. pp. 1259–1262. [4 refs.]

14. Rochaix (A.). L'atténuation du virus fixe par la glycérine et le moyen pratique de l'eviter.—*Ibid.* 1923. Dec. 22. Vol. 89. No. 37. pp. 1309–1310. [1 ref.]

in studying the effects of glycerine. GONSALVES (15) suggests the use of purified olive oil as a preservative, but REMLINGER (16) replies that it has no disinfectant properties.

All these methods are put forward with the object of simplifying the usual Pasteurian technique, and it is satisfactory at this date to know that those who still use it have realized its many disadvantages. Thus MARIE of Paris writes to FERMI of Sassari (17) : "I am convinced as you are, of the necessity of simplifying the procedure of Pasteur . . . I believe that the method of carbolized virus is equally simple and offers many advantages, as would appear from work published and results obtained."

We turn then naturally and with some relief from the above to the consideration of a rabies vaccine prepared according to the ordinary methods in use in vaccine therapy. We shall not discuss in detail the long and acrid controversy (17) which is being waged between FERMI and PUNTONI regarding the use of carbolized virus. It is admitted by all that, even as in the case of other vaccines, a living vaccine has greater immunizing properties than one which has been killed. Disinfection by weak solutions of carbolic acid is a slow process, and at different stages in the process there will be different numbers of survivors. One may with SEMPLE use a virus in which there are no survivors, or with PUNTONI (18) commence with dead, and pass on to emulsions in which there are some survivors. The principles involved are the same, and are in accordance with ordinary practice. Whether living or dead then—and if the dead suffice, then there can be no argument in favour of the living—the method of antirabic inoculation seems at last to be settling on to the simple foundations of the technique of ordinary vaccine therapy.

Carbolized virus is used in Sardinia, throughout India, in Mesopotamia, in Japan, and in Rome.

When the number of patients becomes large the method of PASTEUR becomes impracticable. On the other hand, the consumption of rabbits and the work entailed in the treatment of dried cords becomes too great; on the other, the number of "accidents paralytiques' becomes too obtrusive.

SIMON (quoted by HETSCH) (19) collected information regarding 211,779 persons who had, during the years 1888–1911, undergone treatment by emulsions of dried cords. Of these eighty-four, or 0·48 per thousand, suffered from paralytic accidents. REMLINGER (1905) (quoted by HARVEY and ACTON, *Indian Journal of Medical Research,*

15. GONSALVES (N. Botafogo). Lipovaccination antirabique. Conservation du virus rabique dans l'huile d'olive.—*C.R. Soc. Biol.* 1924. Apr. 4. Vol. 90. No. 12. pp. 876–877. [1 ref.]

16. REMLINGER (P.). L'huile d'olives peut-elle remplacer la glycérine pour la conservation du virus rabique.—*C.R. Soc. Biol.* 1924. June 20. Vol. 91. No. 21. pp. 59–61.. [3 refs.]

17. FERMI (Claudio). Diagnosi biologica della rabbia—Autovaccinazione da virus di strada—Metodo di vaccinazione e di sierovaccinazione. (Replica alla risposta del Prof. V. Puntoni pubblicata negli "Annali d'Igiene." 1923. No. 12.)—*Ann. d'Igiene.* 1924. Feb. Vol. 34. No. 2. pp. 115–122. [3 refs.]
PUNTONI (Vittorio). Risposta al Prof. Fermi.—*Ibid.* p. 123. [1 ref.]

18. PUNTONI (Vittorio). Moderna organizzazione di un Istituto antirabico. L'Istituto antirabico di Roma durante l'ultimo quinquennio.—*Policlinico. Sez. Prat.* 1924. Apr. 14. Vol. 31. No. 15. pp. 482–484. [7 refs.]

19. HETSCH (H.). Die Lyssainfektion und ihre Behandlung.—*Med. Klin.* 1924. Jan. 27. Vol. 20. No. 4. pp. 103–107. [1 ref.]

1923, Vol. X, p 1038) reported forty cases out of a total of 107,712 persons treated (or 0·37 per thousand). No such accidents occur after treatment according to the method Högyes or by carbolized virus (Kasauli, no cases in 47,420).

In the Pasteur Institute at Kasauli 7,506 patients were treated in the year 1920. At the above rate this would entail about three such accidents a year. The reviewer may say from personal experience that neither the nerves nor the reputation of a director could bear such a strain as this. Strain is measured not by percentages but by actual numbers.

A useful modification of antirabic vaccine arises from the application of the method of freezing followed by quick desiccation (SWIFT, *Journal of Exper. Medicine* 1921, Vol. 33, 1). KIRSCHNER (20) describes a modification of SWIFT's apparatus, and claims that after such treatment fixed virus preserves its virulence for sixteen months.

GEDROYC (21) has investigated the action of the lymph of the insect *Deilephila euphorbiae* upon rabies virus and shown that it destroys the parasite in twenty-four hours in vivo.

ARLOING and THÉVENOT (22), following up their investigations on the protective action of proteid and anaphylactic "shock" on tetanus toxin, have turned their attention to rabies. They claim that in the guineapig the gravity of the infection is diminished and the course delayed by such treatment. Their results showed that anaphylactic shock was more effective than protein shock, and that casein peptone was more potent than either horse-serum or muscle-peptone. Experiments on rabbits resulted in complete failure. They ascribe this to the extreme sensitiveness of the rabbit to the fixed virus (rabbit) with which the tests were carried out, and to the feebler reaction of the rabbit as compared with the guineapig to shock of either sort. REMLINGER and BEL (23) have shown that urotropin has no effect upon street virus rabies in guineapigs.

With regard to the clinical aspects of the disease, CHAKRAVERTI (24) describes a case with an incubation period of seven months, and ALBERTYN (25) discusses the diagnosis of probable rabies in a person bitten by a "meerkat." BABÉS and JONESCO (26) draw attention to

20. KIRSCHNER (L.). Over het verduurzamen van Bacteriën en van het Rabies-Virus-fixe. [On the Preservation of Bacteria and of Rabies-Virus-Fixe.]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1924. Vol. 64. No. 2. pp. 193–204. With 1 text fig. [38 refs.]

21. DE GEDROYC (Michal). L'influence de la lymphe des insectes sur le microbe de la rage.—*C.R. Soc. Biol.* 1924. Apr. 4. Vol. 90. No. 12. pp. 906–907.

22. ARLOING (Fernand) & THÉVENOT (Lucien). Essais sur l'action prevéntive et curative des chocs protéiques et anaphylactiques dans la rage expérimentale.—*Bull. Acad. Med.* 1924. June 10. Year 88. 3rd Ser. Vol. 91. No. 24. pp. 733–736. [2 refs.]

23. REMLINGER (P.) & BEL (P.). Inefficacité de l'urotropine comme médicament préventif ou curatif de la rage.—*C.R. Soc. Biol.* 1924. May 23. Vol. 90. No. 17. p. 1312.

24. CHAKRAVERTI (Amulyaratan). A Case of Hydrophobia with unusually Long Incubation Period.—*Calcutta Med. Jl.* 1924. Feb. Vol. 18. No. 8. pp. 622–623.

25. ALBERTYN (C. J.). Rabies?—*S. African Med. Rec.* 1924. Mar. 8. Vol. 22. No. 5. pp. 98–100.

26. BABÉS (V.) & JONESCO (Démètre). Un cas d'hémianesthésie rabique ascendante.—*C.R. Soc. Biol.* 1924. Jan. 25. Vol. 90. No. 2. pp. 144–145.

a case in which symptoms of rabies were preceded by hemianaesthesia. As this case interrupted a long series of successes, and on account of the peculiar clinical picture, they conclude that there is evidence in this instance of a variety of parasite or of toxin which is not influenced by their method of treatment.

With regard to the curability of rabies attention must be directed to an important paper by Rigney D'Aunoy (27). He inoculated six rabbits, each with 500 minimum infective doses of fixed virus. Of these five showed symptoms on the seventh day, three dying on the eighth and two on the ninth. The history of the sixth rabbit is as follows :—It became sick on the seventh day and paralysed in the hind quarters on the eleventh day, on the fifteenth it remained lying down, on the sixteenth it began to improve, and on the seventeenth it could stand up, but was very unsteady. From the nineteenth recovery was rapid, until the twenty-fifth it appeared to be in normal health.

On the sixteenth day when improvement began D'Aunoy drew off some saliva, and injected it into two other rabbits. These developed rabies, the diagnosis being confirmed both by the presence of Negri bodies and by further animal experiments. Saliva was again drawn off on the fortieth day, and injected into two rabbits ; these did not develop rabies, though they were susceptible, as was proved by the fact that they succumbed to a further injection of one minimum infective dose of fixed virus.

On the fortieth day this remarkable animal received 1,000 minimum infective doses of fixed virus subdurably, as also did two controls. The controls died, but the test animal escaped.

Before leaving the subject of animal experiment we may refer to papers by Rochaix and Papacostas (28), who confirm the fact that the mucous membrane of the intestine is impermeable to the virus ; by Isabolinsky (29), who points out that contaminations of cords taken for the purpose of treatment from rabbits are probably of external origin ; by Utenkow (30), describing a method of intracerebral inoculation through the protuberantia occipita externa ; and by Figueira (31), upholding the value of guineapigs as experimental animals for diagnostic purposes.

Cerutti (32) reports cases of canine rabies from German East Africa and Chassigneux (33) from Dakar.

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27. D'Aunoy (Rigney). Spontaneous Recovery of Rabbit from Experimental Rabies.—*Jl. Infect. Dis.* 1924. Apr. Vol. 34. No. 4. pp. 425–427. [7 refs.]

28. Rochaix (A.) & Papacostas (G.). Sur l'imperméabilité de la paroi intestinale pour le virus rabique.—*C.R. Soc. Biol.* 1923. Dec. 22. Vol. 89. No. 37. p. 1308. [1 ref.]

29. Isabolinsky (M.). Ueber die Sterilität des Virus fixe.—*Cent. f. Bakt.* 1 Abt. Orig. 1924. Mar. 25. Vol. 91. No. 6. pp. 396–398.

30. Utenkow (M. D.). Eine neue intrazerebrale Methode der Impfung des Tollwutvirus.—*Cent. f. Bakt.* 1 Abt. Orig. 1924. Apr. 30. Vol. 91. No. 7/8. pp. 490–492. With 1 fig.

31. Figueira (L.). Le cobaye et le diagnostic biologique de la rage.—*C.R. Soc. Biol.* 1924. Mar. 7. Vol. 90. No. 8. pp. 584–585. [1 ref.]

32. Cerruti (G.). Sur plusieurs cas de rage constatés en Afrique Centrale (Urundi).—*Ann. Soc. Belge de Méd. Trop.* Brussels. 1924. Jan. Vol. 3. No. 3. pp. 213–221.

33. Chassigneux (André). A propos de quelques symptômes rabiformes observés chez des chiens à Dakar.—*Bull. Soc. Path. Exot.* 1924. Apr. 9. Vol. 17. No. 4. pp. 325–326.

Some interesting facts regarding the bites of herbivora are detailed by Ouchakoff (34) from Russia. During the period 1902–1914 the registers from all the Russian antirabic stations show 2,859 persons as having been bitten by rabid horses and 3,522 by rabid cows. One of the former group succumbed, and none of the second. It is usually held that rabies cannot be conveyed by the bites of rabid herbivora, but statistics of any magnitude have been difficult to obtain. The value of the Russian figures is that they set an upper limit to the chance of infection. If it exists at all it is less than one-sixtieth per cent.

A. G. McKendrick.

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34. Ouchakoff (V. G.). Les morsures par les herbivores.— *Arch. Biological Sciences.* Petrograd. 1923. Vol. 23. No. 1–3. In Russian. pp. 59–62. [9 refs.] French summary p. 231.

Archives de l'Institut Pasteur de Tunis. 1924. Apr. Vol. 13. No. 1. pp. 138–153.—**Fonctionnement des services de l'Institut Pasteur de Tunis pendant l'année 1923.**

Ceylon. Administration Reports. **Report of the Director, Government Pasteur and Bacteriological Institutes, for the Year 1922.** [Nicholls (Lucius) Director.]—8 pp.

Dolbey (Robert V.) & Abdullah El Katib. **Hydrophobia in Egypt.**—*Lancet.* 1924. Mar. 15. pp. 538–540.

Hajek (K.). [**Nervous Disturbances after Hydrophobia Vaccination.**]—*Zentralb. f. innere Med.* Leipzig. 1924. May 3. Vol. 45. p. 344.

Mikhailof (A.). **La rage et son traitement en Bulgarie.**— *Jl. Physiol. et de Path. Gen.* 1924. Jan. Year 23. Vol. 22. No. 1. pp. 79–82.

Rochaix (A.). **Le traitement antirabique dans la région Lyonnaise. (1922.)** —*Jl. de Physiol. et de Path. Gén.* 1923. Year 22. Vol. 21. No. 4. pp. 722–724.

Szymanowski (Z.) & Sienczewski (St.). **Contribution à l'étude de l'immunisation des chiens contre la rage.**—*C.R. Soc. Biol.* 1924. Mar. 21. Vol. 90. No. 10. pp. 697–699.

Tcheschkoff (A. M.). **La rage dans ses rapports avec la situation alimentaire de Petrograd.**— *Arch. Biological Sciences.* Petrograd. 1923. Vol. 23. No. 1–3. In Russian. pp. 63–69. French summary pp. 232–233.

KALA AZAR.

HANCE (J. B.). **The Geographical Distribution of Kala-Azar.**— *Indian Med. Gaz.* 1924. Feb. Vol. 59. No. 2. pp. 82. [4 refs.]

It is generally believed that kala azar does not occur in the North-West Frontier Province of India. In a number of cases of enlargement of the spleen with irregular fever in the hospital at Dera Ismail Khan the aldehyde reaction gave a positive result. Puncture of the spleen, however, failed to yield Leishmania until recently, when they were discovered in two cases in natives who were born near Kohat and who had never been out of the Province. It is thus evident that the ideas on the geographical distribution of the disease require revision.

C. M. Wenyon.

GANGULI (P.). **Investigations on the Etiology and Treatment of Kala-Azar and some other Common Diseases in Bengal.**— *Indian Med. Rec.* 1924. Feb. Vol. 43. No. 2. pp. 34–36.

From a study of 75 cases of kala azar a number of points of interest came to light. The formol-gel test is more reliable than the globulin precipitate test. The gelification does not as a rule take longer than 20 minutes to occur. It was positive in three minutes in a mild case of splenomedullary leukaemia. Blood serum of early kala azar cases was free from bile ; if present in cases of less than five months' history it was usually due to malaria. Nearly every case of kala azar gave the test for occult blood in the faeces, a fact which the author considers sufficient to account for the anaemia. The specific gravity of the blood in 23 cases examined was below 1,053. In the treatment of cases it was found that if the solution of sodium antimony tartrate was autoclaved before use the febrile reaction which followed the injection of solutions which had been sterilized by boiling could be avoided.

C. M. W.

BASU (Sudhir Chandra). **Age Incidence of Kala Azar Patients.**— *Indian Med. Rec.* 1924. Apr. Vol. 43. No. 4. pp. 107–108. With 1 chart in text.

Of a series of 1,599 cases of kala azar in Bengal, regarded as such because the blood examination was negative for malaria and because they responded to treatment with tartar emetic, 8 per cent. were below 5 years of age, 29 per cent. between 5 and 10, 23 per cent. between 10 and 15, 17 per cent. between 15 and 20, 14 per cent. between 20 and 30, 7 per cent. between 30 and 40, and 2 per cent. over 40.

C. M. W.

BANERJEE (Dhirendra Nath). **The Latent Phase of Kala-Azar.**— *Calcutta Med. Jl.* 1924. Mar. Vol. 19. No. 9. pp. 655–658. (Discussion pp. 658–660).

The author draws attention to obscure cases of kala azar in which there may be little fever or enlargement of the spleen and absence of the classical symptoms of the disease. Writing of medical practice

in Bengal he states that all cases of anaemia and diarrhoea or dysentery with or without fever or enlargement of the spleen should be looked upon with suspicion.

C. M. W.

MAITRA (Jitendra Nath). **A Flagellate found in the Peripheral Blood Smear of a Case clinically one of Kala-Azar.**—*Calcutta Med. Jl.* 1924. Feb. Vol. 18. No. 8. pp. 618–619. With 1 plate.

The paper records the discovery in a blood film of a female patient, 16 years of age, in the surgical wards of the Campbell Hospital, Calcutta, of a flagellate having the characters of a leptomonas. The patient had an enlarged spleen, was anaemic, and her case clinically resembled one of kala azar. The serum globulin test was positive. It was not possible to confirm the diagnosis of kala azar and blood films made later did not reveal any more flagellates. Contamination of the film from the distilled water is regarded as excluded, as other films stained on the same day did not show the flagellates. A coloured plate shows three of the organisms, which are indistinguishable from cultural forms of leishmania. [It is particularly unfortunate that the case could not be thoroughly examined. One possible source of error, not mentioned, is the deposit on blood films of similar flagellates by house flies which have access to them. The reviewer knows of at least one case where such a contamination took place. It is perhaps worthy of note that the reviewer on one occasion found flagellate stages of leishmania in a spleen smear of a dog experimentally infected with *L. donovani* (this *Bulletin*, Vol. 7, p. 81).]

C. M. W.

BANERJEE (Dhirendra Nath). **Observations on the Occurrence of Leishmania in Ulcers of Stomach in a Case of Kala-Azar.**—*Calcutta Med. Jl.* 1923. Sept. Vol. 18. No. 3. pp. 385–388. With 1 plate. [7 refs.]

A Hindu female, aged about 45, admitted to hospital for anaemia, subsequently died of diarrhoea and malnutrition; post mortem 120 ancylostomes were found in the intestine and it was thought the case was one of ancylostomiasis. On examination of smears of the bone marrow the author was surprised to find a large leishmania infection. Parasites were subsequently found in smears of the spleen and liver and in scrapings from a number of ulcers which occurred in the posterior wall of the stomach. The last observation appears to the author to lend support to the view that kala azar is acquired by way of the alimentary canal.

C. M. W.

ELWES (F. F.), MENON (V. K. Narayana) & RAMAKRISHNAN (P. S.). **The Formol-Gel (Aldehyde) Test as a Means of Diagnosis of Kala-Azar.**—*Indian Med. Gaz.* 1924. Apr. Vol. 59. No. 4. pp. 175–177. [6 refs.]

Out of a total of 81 proved cases of kala azar no less than 23·4 per cent. gave a completely negative formol-gel test, and 12·3 per cent. gave a doubtful reaction. Thus in 35·7 per cent. of the cases the test was of little or no value. Furthermore, there is a certain group of

cases which clinically appear to be kala azar and give a positive formol-gel reaction and react to potassium antimony tartrate, though leishmania cannot be discovered by liver puncture. It is doubtful if these cases are true kala azar.

In a note to this paper by NAPIER, it is pointed out that the formol-gel test has its limitations and that it depends largely on the duration of the disease. In early stages when parasites are numerous the reaction may be negative because normal metabolism has not yet been deranged, while it may be positive in treated cases which have completely lost their symptoms and all trace of parasites. It is thought that the suggestion that the cases showing symptoms of kala azar may be some other disease is extremely hypothetical and merely rests on an inability to find the parasites by liver puncture. In cases in which the parasites are scanty in the material obtained by spleen puncture it is usually impossible to find them by liver puncture. In certain cases as many as four spleen punctures have been performed without finding parasites by microscopical examination of smears, though a positive diagnosis has eventually been obtained by culture.

C. M. W.

STRUTHERS (E. B.) & CH'I CHANG CH'UN. **The Globulin Precipitation and Formol-Gel Tests in the Diagnosis of Kala-Azar.**—*China Med. Jl.* 1924. Mar. Vol. 38. No. 3. pp. 203–206. With 1 fig. [7 refs.]

The globulin precipitation test and the formol-gel test were applied to 141 cases of kala azar in China, all of them diagnosed by the discovery of leishmania, except one which was obviously this disease from the clinical features and the response to tartar emetic treatment. Only reactions decidedly positive were accepted. Of these 141 cases 92·9 per cent. gave a positive reaction with the globulin test and 98 per cent. with the formol-gel test. In 77 cases of other diseases the formol-gel test was uniformly negative. The cases of kala azar which failed to give a reaction were early ones, a result similar to that obtained by NAPIER in India. The globulin test employed was that of RAY and was carried out by adding from a pipette 2 drops of blood to 20 drops of distilled water in a test tube. If the test is positive a flocculent precipitate appears in a few minutes.

C. M. W.

DE CAPITE (A.). **Sulla gelatinizzazione del siero di sangue nella leishmaniosi infantile.**—*Pediatria.* 1924. Apr. 1. Vol. 32. No. 7. pp. 408–413. [16 refs.]

The author has used the formol-gel test in 18 cases of active kala azar, two cases of recovered kala azar, seven cases of splenic anaemia and 30 cases of illness due to other causes. Though the reaction may not be so rapid as NAPIER observed, the author is convinced of its reliability as a diagnostic procedure in kala azar. He does not claim that it can be expected to render search for the parasite unnecessary, but he considers it sufficiently accurate to justify a probable diagnosis of the disease. In the eighteen cases the reaction was obtained in 1 case in 10 minutes, in 2 in 15 minutes, in 4 in 30 minutes, in 2 in 45 minutes, in 3 in 1 hour, in 3 in 2 hours, in 1 in 4 hours, and in 2 in 6 hours. In 3 of the other cases in which it was obtained the time limit was 24 hours.

C. M. W.

Sarkar (Sarasi Lal) & De (Anath Bandhu). **Some Observations on the Aldehyde Test.**—*Calcutta Med. Jl.* 1923. Dec. Vol. 18. No. 6. pp. 539–543.

Though it is concluded that the aldehyde test in certain cases of kala azar was a much delayed reaction, the results are invalidated by the fact that none of the cases were diagnosed by the discovery of leishmania. On this account also the remark that about one-third of kala azar cases undergo slow spontaneous recovery is of little scientific value.

C. M. W.

Brahmachari (U. N.), Chaudhury (Saroda Charan), Das (Judhistir) & Sen (Parimal Bikas). **Chemotherapy of Antimonial Compounds in Kala-Azar Infection. Part VIII. Quantitative Studies in Excretion of Antimony (Tartar Emetic and Urea Stibamine).**—*Indian Jl. Med. Res.* 1924. Jan. Vol. 11. No. 3. pp. 829–838. With 1 chart.

The authors have investigated the rate of antimony excretion after intravenous injections of tartar emetic and urea stibamine. In the case of tartar emetic the quantity excreted in the urine during the first 24 hours is about 6 per cent. of the amount injected; in the case of urea stibamine it is 30 to 40 per cent. The actual quantity excreted is fairly proportional to the amount injected and is independent of the quantity of urine passed. If a pentavalent antimony compound is injected the excretion during the first 24 hours is rapid, after which it is slower and follows the rate of excretion of a trivalent compound.

It is probable that in the body a pentavalent compound is reduced to a trivalent one and that so long as it remains in the pentavalent condition the excretion is rapid. Antimony may be present in the urine for two months after a single injection of an antimony compound. In the case of urea stibamine where the greater portion of the antimony is in a pentavalent condition the chances of toxicity from such a drug are less than from antimony tartrate. It is probable that during the conversion of a pentavalent to a trivalent compound a reactive —Sb = O radicle is formed, which may perhaps explain the remarkably good results following the use of urea stibamine. The quantity of antimony excreted by the faeces is irregular and considerably less than that excreted in the urine. These observations, together with the fact that its therapeutic value is very great, make urea stibamine the best of all the antimonial compounds that have so far been discovered for the treatment of leishmaniasis, and other diseases in which antimony is indicated.

C. M. W.

Brahmachari (U. N.). **Chemotherapy of Antimonial Compounds in Kala-Azar Infection. Part IX. Treatment of Cases of Kala-Azar Resistant to Antimonyl Tartrates with Urea Stibamine—the Therapeutic Value of Stibamine in Kala-Azar.**—*Indian Jl. Med. Res.* 1924. Apr. Vol. 11. No. 4. pp. 1,205–1,217.

The author describes his experiences with urea stibamine in the treatment of 9 cases of kala azar which had proved resistant to treatment with antimonyl tartrate; all responded at once to urea stibamine, and it is worthy of note that the course of curative treatment was shorter and the number of injections less than is usual with antimonyl tartrate. No case of kala azar met with up to the present has resisted treatment with urea stibamine, and some of the cases have been under

observation for nearly 2 years after completion of the course. In the treatment of the 9 cases referred to the doses of the drug varied as follows :—1. Nine injections of 0·2–0·25 gm. twice a week. 2. Eight injections of 0·2 gm. twice a week. 3. Total of 3·5 gms. in 15 injections twice a week. 4. Nine injections of 0·1–0·25 gm. (total 1·6 gms.) in 1½ months. 5. Total of 3·0 gms. in 12 injections on alternate days. 6. Total of 2·2 gms. in 9 injections during 2 months. 7. Total of 2·4 gms. in 10 injections during 1½ months. 8. Doses of 0·1 to 0·25 gm. (total 2·8 gms.) in 13 injections during 2 months. 9. Total of 2·2 gms. in 12 injections during 1½ months.

It is noted that a further series of 6 cases which have resisted more than 4 gms. of tartar emetic or sodium antimonyl tartrate are rapidly improving under urea stibamine.

Both the author and Major SHORTT are testing the drug by intramuscular injection. The local reaction is generally very slight and it is possible that the drug may be used with advantage in this way.

An account of 3 cases treated with stibamine is also given. It is noted that unless the salt is perfectly neutral its solution in water is likely to decompose. The pure salt is fairly stable. The following doses were given :—1. Total 2·4 gms. in 20 injections during 54 days. 2. Total 1·2 gm. in 18 injections during 48 days. 3. Total 4·4 gms. in 30 injections during 100 days. All the cases were apparently cured.

C. M. W.

GERSCHENOWITSCH (R. S.). [**On the Comparative Value of Existing Methods of Treatment of Infantile Leishmaniasis.**]—*Russian Jl. Trop. Med.* Moscow. 1924. No. 2. pp. 11–16. [40 refs.] [In Russian].

The author had 25 cases of infantile leishmaniasis under observation, seven of which were treated with tartar emetic alone, by ROGERS' method, and eighteen by the combined method introduced by SLONIM. In the latter a dose of neosalvarsan is injected after every 4–5 injections of tartar emetic. The usual doses of both salvarsan and antimony were employed. In the series treated by ROGERS' method 3 cases recovered and 4 died, whereas in the series treated by SLONIM'S method 14 recovered and 4 died. The average number of injections of tartar emetic was 35 in cases treated according to ROGERS, and 25 in those treated by SLONIM'S method. The course of treatment by both methods lasted on the average 3–3½ months.

The author notes that the blood improves very slowly when antimony alone is used. The addition of neosalvarsan, however, causes a rapid improvement in the cell content and raises the haemoglobin index, the coagulability and the alkalinity.

C. A. Hoare.

STRUTHERS (E. B.). **Kala-Azar : Criterion of Cure.**—*China Med. Jl.* 1924. Mar. Vol. 38. No. 3. pp. 207–212. [4 refs.]

Since the adoption of the tartar emetic treatment for kala azar cases at the Shantung Christian University Hospital, Tsinan, China, the writer of the paper has experienced a difficulty in deciding when a case can be regarded as cured. It is concluded that at present there is no certain criterion of cure unless the failure to cultivate parasites from spleen material be so considered. The globulin precipitation test and the aldehyde test cannot be relied upon as indications of cure.

The most satisfactory indication appears to be increase in general well-being and weight, a return to normal temperature continuous for a month or six weeks, a decrease in the size of the spleen, and an increase in the leucocytes and haemoglobin of the blood. Prolonged treatment for three to five months is necessary.

Of 37 discharged patients who reported that they were in good health, 21 have been well for 2 to 6 months and 16 from 6 to 12 months. The general results for 100 patients discharged between January 1922 and November 1923 were as follows :—Cured, 61 ; improved (treatment incomplete), 18 ; died 21. The high death rate is accounted for by the fact that there was no refusal of cases in the last stages of the disease, many of whom died shortly after admission. The treatment adopted is on the lines of that recommended in India.

C. M. W.

Shortt (H. E.) & Swaminath (C. S.). **Note on the Infection of a Mouse by Means of Bed-Bugs, *Cimex hemiptera* Fabr., fed on the Peripheral Blood of a Case of Kala-Azar.**—*Indian Jl. Med. Res.* 1924. Jan. Vol. 11. No. 3. pp. 965–966.

It is rare to find flagellates in bugs which have fed on the peripheral blood of kala azar cases solely by direct microscopical examination, but their presence can often be demonstrated by the cultural method. They are present at first in the mid-gut, but the longer the infection lasts the more do they tend to migrate towards the hinder end of the gut, where they may be detected long after they have entirely disappeared from the mid-gut. These forms are presumably passed in the faeces and may conceivably cause a new infection if introduced into the puncture wound. To test this point, bugs were fed on kala azar cases which showed parasites in the peripheral blood. They were dissected nine days later and the guts were emulsified in saline and injected intraperitoneally into mice. The minimum period of 9 days was chosen, as it had been found that flagellation of the ingested parasites occurs in 3 to 6 days, and it was presumed that at the 9th day all the forms present would be in the flagellate condition. Of five mice which were inoculated with the emulsion of 12 to 20 bug intestines one gave a positive result on the 123rd day. Direct examination of smears showed no parasites, but a culture was obtained from the spleen. No leishmania were obtained from the others, but the examinations were not satisfactory. One died in 24 hours after the inoculation, one was found dead with bacterial contamination of the organs, one gave only contaminated cultures, while one was killed in moribund condition from an undetermined cause on 37th day. It is thus demonstrated that 9 days after feeding on a kala azar case the intestine of bugs may contain leishmania which are infective to mice.

C. M. W.

Smyly (H. Jocelyn) & Young (Charles W.). **The Experimental Transmission of Leishmaniasis to Animals.**—*Proc. Soc. Experim. Biol. & Med.* 1924. Mar. Vol. 21. No. 6. pp. 354–356.

Young (Charles W.), Smyly (J. Jocelyn) & Brown (Cabot). **Experimental Kala-Azar in a Hamster (*Cricetulus griseus*, M.-Edw.).**—*Ibid.* pp. 357–359. [1 ref.]

These two papers may be considered together as both deal with the marked susceptibility of the Chinese hamster (*Cricetulus griseus*,

M.-Edw.) to *Leishmania donovani*. It is noted that the lack of an animal which can be readily and surely inoculated with *L. donovani* has been a serious obstacle to investigation work and it is hoped that in the hamster many of the difficulties may be overcome. The first paper describes the inoculation of a series of animals with material from emulsified spleen of a heavily infected case. Two dogs were inoculated intravenously with 5 and 4·5 cc. of the saline suspension, while 2 guinea-pigs, 2 white rats, 2 black mice and 5 hamsters were inoculated intra-peritoneally with 0·3 to 0·5 cc. The results obtained in these animals were as follows. One dog gave a positive blood culture on the 38th day ; it died later but no autopsy was made. The other dog also gave a positive blood culture on the 42nd day ; after 4½ months the spleen, at autopsy, was found infected. The guineapigs were negative at autopsy on the 95th and 131st days, as also were the white rats on the 29th and 90th days. The black mice were positive on the 111th and 121st days. All the 5 hamsters were positive on the 8th, 45th, 116th and 351st days.

A second series of animals was inoculated from a case with light infection as follows :—2 dogs with 10 cc. and 5 cc. of spleen emulsion, 2 dogs with 10 cc. and 5 cc. of liver emulsion, 1 hamster with 1 cc. of spleen emulsion, 2 with 1 cc. of liver emulsion and 2 with 1 cc. of marrow emulsion. All the dogs were examined by liver and sternum puncture on 102nd to 107th day with negative result. One hamster was examined by autopsy on 105th day ; the spleen was infected. Liver puncture performed on three hamsters gave a positive result, as also did their examination at autopsy on 116th and 144th days ; a liver puncture was performed on the 5th hamster on the 131st day with positive result.

The second paper is a continuation and confirmation of the first. Of 89 hamsters inoculated intraperitoneally infection was demonstrated in 91 per cent. Intracellular organisms were found in the animals at varying intervals from 1 to 332 days after inoculation. To ascertain whether the organisms came from the tissues or from the unabsorbed material in the peritoneal cavity, 20 animals were inoculated and 4 were examined at daily intervals. In each animal the following smears were examined :—1. centrifuged peritoneal washings ; 2. liver rinsed twice to free it from inoculum ; 3. similarly washed spleen ; 4. bone marrow (femur). Intracellular parasites were found in the peritoneal cavity throughout the five days. They appeared first in the spleen (3 days) and then in the liver and bone marrow (4 days). In 2 other hamsters intracellular parasites were found in the peritoneal cavity as well as in the washed liver and spleen on the 9th day. Two hamsters inoculated intrapleurally became infected, as also did 2 out of 4 inoculated subcutaneously. Five hamsters were fed on infected material. Two of these died in 8 hours and one in 7 days. Two others were killed on the 18th day. All were negative.

As regards these infections it is noted that there was no tendency towards spontaneous recovery, the infection being progressive in its intensity.

C. M. W.

BANERJEE (Dhirendra Nath). **Cultivation of** *Leishmania donovani*.—*Calcutta Med. Jl.* 1923. Sept. Vol. 18. No. 3. pp. 417–420.

After a summary of the various methods of culture of *Leishmania donovani* the author states that in his laboratory the best results have

been obtained by Row's method. A half to 1 cc. of blood is placed in 20 cc. of citrate saline solution. After mixing thoroughly the tube is incubated for 24 hours at 22°C. With the sediment which has then formed tubes of N.N.N. medium are inoculated in the usual manner.

C. M. W.

NAPIER (L. E.). **The Reaction of the Blood in Kala Azar.**— *Indian Jl. Med. Res.* 1924. Jan. Vol. 11. No. 3. pp. 719–732. With 2 figs. and 5 graphs. [7 refs.]

Though it is generally known that the blood of kala azar cases shows a reduced alkalinity, the author repeated the investigation by the more accurate method for the determination of its hydrogen-ion concentration, using a slight modification of the colorimetric method suggested by DALE and EVANS. It was found that there is actually little change in the pH of the blood in this disease, and that slightly towards the alkaline side, the mean of the blood of 18 kala azar patients and 10 normal persons being 7·379 ± 0·065 and 7·329 ± 0·0415 respectively.

As a consequence the author has elaborated a colorimetric method of estimating accurately the pH of slightly coloured fluids of pH between 1·08 and 11·08. It is a combination of the methods described by DALE and EVANS (1920) and by EVERS (1921), and is applicable not only to blood, but also to urine and faeces. A new form of comparator is also described. The effect of the addition of various quantities of acid and alkali to the blood was studied. It was shown that in kala azar blood the power of neutralizing acid as well as alkali was reduced, so that it would be more accurate to state that in kala azar the " buffer " action of the blood is reduced. The paper is illustrated by a series of tables and charts.

C. M. W.

NAPIER (L. E.). **The Preparation of N.N.N. Media of Different Hydrogen-Ion Concentrations.**— *Indian Jl. Med. Res.* 1924. Jan. Vol. 11. No. 3. pp. 733–736. With 6 graphs.

As a preliminary to the study of the optimum pH conditions of N.N.N. medium for the cultivation of *Leishmania donovani*, the possibility of preparing media of various known hydrogen-ion concentrations and the changes which occur in the medium from day to day were investigated. It was found that the hydrogen-ion concentration changes from pH 7·7 on the day that it is made to pH 7·0 on about the eighth day, after which it increases so slowly that it can be regarded as constant. Medium of any hydrogen-ion concentration from pH 3·5 to pH 8·65 can be prepared by the addition of various quantities of N/10 HCl or N/10 NaOH to ordinary N.N.N. medium before it has " set."

C. M. W.

NAPIER (L. Everard) & MURUGESAN (P.). **The Viability of the Flagellate Stage of *L. donovani* with Reference to the Hydrogen-Ion Concentration of its Environment.**— *Indian Jl. Med. Res.* 1924. Apr. Vol. 11. No. 4. pp. 1219–1226. [6 refs.]

The authors, availing themselves of the results of the investigation just recorded, tested the effect of hydrogen-ion concentration in

N.N.N. medium on the growth of *Leishmania donovani*. They found that on the acid side growth occurs consistently down to pH 4·75; it occurs with less certainty at pH 4·55, while at pH 4·3 the flagellates are killed in 3 days. On the alkaline side the results are less consistent. Growth occurs at pH 8·38 fairly regularly, but much less so at pH 8·6 and apparently not at all at lower concentrations than this. The optimum appears to be pH 5·7 on the acid side and pH 7·3 on the alkaline side. The range over which growth will occur is pH 4·5 to pH 8·6.

It has been found that leishmania will remain alive in the stomach of the frog for 24 or even 48 hours but that in the rabbit death occurs almost immediately. The pH of the stomach contents of the frog is about 6·4 and that of the rabbit below 3·6, the mashed mucous membrane having a pH of 4·5.

The hydrogen-ion concentration of gastric juice of a healthy European is usually greater than pH 2·0, but that of the rice eating Indian is distinctly less and in conditions of ill-health may be as low as pH 6·0. That of the gastric juice of a breast-feeding infant is said to be about 5·0. The authors think that the experiments prove that the hydrogen-ion concentration of the stomach of man under certain conditions is such that it does not negative the possibility of the survival of flagellates in it.

C. M. W.

Tanabe (Misawo). [**On the Conditions Necessary for the Development of *Leishmania donovani* in Vitro.**]—*Saikingaku Zasshi* (*Jl. of Bact.*). 1923. June. No. 333. [Summarized in *Japan Med. World*. 1924. Feb. 15. Vol. 4. No. 2. p. 46.]

The author has cultivated *Leishmania donovani* in the following medium. One part of defibrinated rabbit's blood is mixed with an equal quantity of distilled water. After complete laking 1 part of citrated saline solution (distilled water 900 cc., sodium chloride 12 gms., sodium citrate 10 gms.) is added. The resulting fluid separated in small tubes constitutes the medium. The blood of the dog can be used in place of rabbit's blood, but human and ox blood give less satisfactory results. The blood of the rat, guineapig, horse, goat and monkey were useless. The best results are obtained when rabbit's blood is present in 20–50 per cent. Neither the serum of rabbit's blood alone nor the erythrocytes alone can be used as a substitute for the whole blood. Oxygen appears to exercise no influence on the growth. A neutral medium is the best and no growth occurs if the medium is rendered alkaline or acid by the addition of 10 per cent. normal soda or hydrochloric acid solution. Both potassium chloride and calcium chloride can take the place of the sodium salt. The optimum temperature of growth was 22–25° C.

C. M. W.

De (Monindra Nath). **A Simple Method of staining *Leishmania donovani* in Tissues.**—*Indian Med. Gaz.* 1924. Feb. Vol. 59. No. 2. pp. 82–84. With 1 fig.

For staining Leishmania in sections the following method is recommended. Small pieces of tissue about 0·5 cm. thick are placed in acetone, which is changed every five minutes till the tissue is clear. It is then placed in xylol, when it becomes perfectly clear and transparent, after which it is put in the paraffin bath at 60°C. for about half an hour. After embedding, sections 2–3 microns thick are cut

and these are brought into water in the usual way. They are then stained by Giemsa or Leishman stain as in the case of an ordinary blood film. Excess of stain is washed away with water, and the sections are rapidly dehydrated with acetone, cleared in xylol and mounted in cedar oil.

C. M. W.

BARBERI (Salvatore). **Restauro dei proteici del plasma nel Kala-azar.**—*Pediatria.* 1924. Apr. 1. Vol. 32. No. 7. pp. 399–407. [3 refs.]

From an examination of four cases of infantile kala azar in Italy the author finds that the protein content of the blood is reduced. As recovery takes place improvement in the protein content can be observed before the blood count shows any change for the better.

C. M. W.

i. MUKHERJEE (H. N.). **Calcium Content of Blood in Kala-Azar. A Preliminary Note.**—*Calcutta Med. Jl.* 1923. Sept. Vol. 18. No. 3. pp. 394–396. [3 refs.]

ii. BANERJEE (Dhirendra Nath). **A Scheme for the Control of Kala-Azar in Bengal.**—*Indian Med. Rec.* 1924. Feb. Vol. 43. No. 2. pp. 36–38.

iii. GIRAUD (Paul) & ZUCARELLI (J.). **Le kala-azar infantile autochtone dans la région méditerranéenne.**—*Paris Méd.* 1924. Mar. 22. Vol. 14. No. 12. pp. 278–281. [9 refs.]

iv. AKAMATSU (Tokujiro). [**On Kala-Azar in Shangtung District in China.**] —*Jikken Igaku Zasshi* (*Jl. Experim. Med.*). 1923. Dec. Vol. 7. Nos. 11/12. [Summarized in *Japan Med. World.* 1924. Mar. 15. Vol. 4. No. 3. p. 79.]

v. IGLESIAS GARZA (Tomas). [**Una endemia grave de leishmaniosis infantil en España.**]—*Siglo Méd.* 1923. Nov. 24. [Summarized in *Rev. Española de Med. Cirug.* 1924. Mar. Vol. 7. No. 69. p. 163.]

i. From an examination of the blood of ten cases of kala azar and five normal individuals it was found that in kala azar there was a calcium deficiency which it is thought may account for the decrease in the coagulability of the blood in this disease.

ii. The scheme advocated is the proper training of local practitioners in the methods of diagnosis and treatment of kala azar so that the large number of cases in Bengal can be dealt with.

iii. It is evident that Marseilles is an endemic centre of infantile kala azar, for in addition to the four cases previously noted (this *Bulletin* Vol. 21, p. 253), a fifth case has come to light. The paper describes the five cases in detail, but gives no new information about the disease.

iv. A note stating that the author has discovered kala azar to be endemic in the Shantung Province of China.

v. A note calling attention to the existence of infantile kala azar in Spain.

C. M. W.

BONNE (C.). **La leishmaniose cutanée dans la Guyane hollandaise.**—*Bull. Soc. Path. Exot.* 1924. Apr. 9. Vol. 17. No. 4. pp. 293–295.

In Dutch Guiana the leishmania infection is found in the following forms :—(1). Non-ulcerating papule about the size of a franc piece. (2). Ulcer with a diameter of 1-6 cm. and forming an abundant

secretion: this is the usual type. (3). Eczematous type only seen once. (4). Lymphangitic type with the lymphatics draining an ulcerated area thickened at intervals into nodules which may break down and give rise to secondary ulcers. (5). Hypertrophic type in which large protuberant masses of a papillomatous nature are formed. (6). Mucosal type in which the nasal and buccal mucosae are involved.

All these types respond very readily to treatment with tartar emetic in 3 to 6 weeks, except the hypertrophic variety, which is very resistant and may require months of treatment. The disease, which is only contracted in the forest, is ascribed by the natives to the latex-containing spines of certain lianas. About 100 ticks (Amblyomma) fed on cases during several weeks did not yield evidence of any development of leishmania nor were cultures of the flagellate obtained from the stomach contents of ticks. A species of Phlebotomus (*P. squamiventris* Lutz and Neiva) occurs in the forests. Four specimens were obtained. They were crushed in saline and inoculated by scarification into the skin, but no infection resulted.

C. M. W.

Sergent (Et.) & Gueidon (E.). **Chronique du bouton d'Orient en Algérie. Le " Clou de Mila."**—*Arch. Inst. Pasteur d' Algérie.* 1923. Vol. 1. No. 1. pp. 1–3. [1 ref.]

The authors have been able to demonstrate that the disease long known in Algeria as " Clou de Mila " is oriental sore. Two cases were observed and leishmania were discovered in both. These are the 5th and 6th cases of oriental sore which have been seen in Algeria outside the Sahara district. Forty years ago the disease was so common at Mila that it received its distinctive name, but for some reason not properly understood it has gradually become less frequent, though the town itself with a population of 2,000 has undergone no visible change in the interval. The sand fly *Phlebotomus papatasii* exists, but whether any restriction of its breeding facilities has occurred cannot be stated.

C. M. W.

Montenegro (João). **Inoculabilidade da leishmaniose.**—*Bol. Soc. Med. e Cirurg. de S. Paulo.* Brazil. 1923. Nov. Vol. 6. 3rd. Ser. No. 9. pp. 113–117.

————. **The Inoculability of Leishmania.**—*Amer. Jl. Trop. Med.* 1924. May. Vol. 4. No. 3. pp. 331–340. With 3 figs.

Though autoinoculation was supposed to account for the appearance of secondary lesions in the case of cutaneous leishmaniasis in S. America, the author determined to test this assumption by experimental means. A series of 7 cases of the disease was chosen and autoinoculation of the skin by scarification with material from a skin lesion was carried out on seven occasions. Though 4 of these inoculations caused the appearance of nodules, which never persisted for more than 3 weeks, in only one were definite leishmania discovered. One of the cases had a lesion of the nasal mucosa and with scraping from this an autoinoculation of the skin was performed as well as the inoculation of the skin of another case. There was no result from either of these experiments, nor from the inoculation of the skin of another case with

a culture of leishmania rich in flagellates. Though the majority of the experiments gave inconclusive results, the positive one justifies the conclusion that autoinoculation can take place.

C. M. W.

MARZINOWSKY (E. I.) & SCHOURENKOFF (A. I.). [**Immunity in Oriental Sore.**]—*Russian Jl. Trop. Med.* Moscow. 1924. No. 2. pp. 17–24. With 2 figs. [35 refs.] [In Russian.]

A series of experiments on oriental sore were conducted with the view of elucidating the question of immunity in man. The authors repeatedly inoculated themselves in the arm from naturally infected cases in Turkestan, and summarize the results as follows :—

(1). The incubation period after the first experimental infection is about two months (60–70 days) ,
(2). Repeated inoculations from man to man reduce the period of incubation to a fortnight ;
(3). The course of experimental infection is similar to that of natural infection ;
(4). An experimental sore confers a distinct immunity only in those cases in which the resulting sore is allowed to run a natural course, and heal on its own account ;
(5). Abortive forms of oriental sore in natural infections confer no immunity, which explains the cases of repeated infections described in the literature.

C. A. Hoare.

MONTENEGRO (João). **Anatomo-pathologia da leishmaniose cutanea. (Ulcera de Baurú.)**—*Bol. Soc. Med. e Cirurg. de S. Paulo.* Brazil. 1924. Jan. Vol. 6. 3rd Ser. No. 11. pp. 132–135 ; and *Ann. Paulist. Med. e Cirurg.* 1924. Jan. Year 12. Vol. 15. No. 1. pp. 5–11.

A histological examination of the type of cutaneous leishmaniasis known as ulcer of Baurú leads the author to the following conclusions. The lesion is a granuloma in which plasmocytes, lymphocytes and endothelial cells occur in varying proportions. In indolent lesions and during cicatrization gigantocytes occur. There is no definite necrosis or suppuration. Though the histological characters are not peculiar to the leishmania infections they nevertheless enable one to differentiate them from the common mycotic lesions. Certain syphilitic lesions cannot be distinguished from those due to leishmania.

C. M. W.

KLIGLER (I. J.). **On the Cultivation and Biological Characters of *Leishmania tropica*.**—*Amer. Jl. Trop. Med.* 1924. Jan. Vol. 4. No. 1. pp. 69–76. [4 refs.]

This paper gives an account of oriental sore as it occurs in and around Jericho. Of five cases studied each had two or more sores. CANNAN had already noted in 26 cases that a single sore was the exception. In the five cases studied by the author the parasites appeared to be scantier than they were in a case from Aleppo and another from Baghdad. Cultivation of the organism was effected in a medium differing from that used by NOGUCHI for the cultivation of *Leptospira icteroides* only in the addition of whole blood of the rabbit in place of

serum. It was found that *L. tropica* was very sensitive to changes in reaction, for at pH 7·8 and 6·6 respectively there was no growth. The best reaction is pH 7·2. The tests were made in media the reaction of which was adjusted by hydrochloric and acetic acids, unbuffered, or buffered with phosphate. For sub-cultures it was found that NOGUCHI's serum medium was very satisfactory and that under a layer of paraffin at a temperature of 22°–25°C. cultures would remain alive for at least 6 months. The effect of various drugs on the growth of *L. tropica* was tested. It was found that after 2 weeks' incubation a medium containing 1 : 20,000–1 : 40,000 tartar emetic showed active flagellates, while that containing 1 : 10,000 did not. The figures for brilliant green, salvarsan and neosalvarsan were 1 : 400,000 and 1 : 200,000, 1 : 25,000 and 1 : 20,000 and 1 : 33,000 and 1 : 25,000 respectively.

[The cultivation of Leishmania in a medium similar to that described by the author has been previously noted. *Trans. Roy. Soc. Trop. Med. Hyg.* xv. 153 (WENYON).]

C. M. W.

MANGIN. **Au sujet du traitment du bouton d'Alep.**—*Bull. Soc. Path. Exot.* 1924. May 14. Vol. 17. No. 5. pp. 361–367.

A stay of 15 months in Aleppo gave the author an opportunity of studying the local form of oriental sore and of elaborating a method of treatment which has given such good results that he is led to describe it. The treatment adopted in any particular case depends on the condition of the sore and is based on the use of the following mixtures :—

Mixture I	..	Extrait de Javel (?Javelle water)	25 gms.
		Glycerine	100 gms.
Mixture II	..	Mixture I	1 part.
		Glycerine	4 parts.
Mixture III	..	Mixture I	1 gm.
		Lanoline	40 gms.

Lesions in the early papule stage are treated with hot applications of a 10 per cent. dilution of Mixture I till there is formed a scab which is scraped off. The sore is curetted and Mixture I is applied, but on a cotton wool plug, which is fixed in by dressing and bandage. This is repeated on 5 to 8 successive days.

Sores in the vesico-pustular condition are similarly treated, the cavity being cleaned out each day and the soaked cotton wool plug being brought into contact with the edge in which parasites develop. Usually the infection is arrested on the sixth day, after which dressings of Mixture II or III are used. Fully developed ulcers are treated in the same manner, after removal of the scabs. It is advisable to dry the cavity carefully before making the application and to cover the skin outside the ulcer with lanoline or other ointment to prevent autoinoculations. If sores are in the healing period with signs of cicatrization Mixture II or III can be employed. In the final stages application of Lugol's solution is often advantageous. Occasionally abnormal lesions of non-ulcerating type are met with. These are treated with hot applications of the mixture repeated till an open sore is formed, when the dressings are applied to the interior. It may be necessary to lance the sore. Sores on the mucous membranes,

which are often multiple in the form of small ulcers, are satisfactorily treated with applications of bismuth salicylate. A severe case was seen in which the whole upper lip was involved.

The advantages of the line of treatment described above are :—

1. Economy ; 2. Painlessness ; 3. Clean, practical and rapid ; 4. Action only on the infected tissue and not on the healthy skin ; 5. Without danger. Of 54 cases thus treated cure was effected in 8 to 30 days.

In Aleppo oriental sore is most frequently met with at the end of the summer. Dogs are liable to infection on the nose and 3 cases treated were cured rapidly.

C. M. W.

MAZUMDAR (D. C.). **Notes on the Treatment of Oriental Sore by Intravenous Injections of Antimony Tartrate.**—*Indian Med. Gaz.* 1924. May. Vol. 59. No. 5. p. 238.

The author records his experiences in the treatment of oriental sore in the Indian General Hospital at Dera Ismail Khan during the year 1920–1921. About 300 cases were dealt with, and it was found that the best results were obtained by the use of intravenous tartar emetic combined with strong saline dressings on the sores. The average stay in hospital was 4 to 6 weeks.

C. M. W.

SERGENT (Et.), GUEIDON (E.), BOUGUET (A.) & CATANEI (A.). **Existence de la leishmaniose cutanée chez le chien dans une localité du Tell algérien où le bouton d'Orient est endémique chez l'homme.**—*Bull. Soc. Path. Exot.* 1924. May 14. Vol. 17. No. 5. pp. 360–361. [2 refs.]

Having discovered that the " Clou de Mila " in Algeria was actually oriental sore, as announced above, the authors noted that a dog in the same locality had ulcers in its nose and internal surface of both ears. Scrapings from these lesions showed numerous leishmania. This is the first demonstration of cutaneous leishmaniasis in dogs in the Mediterranean area. It has previously been discovered in dogs in Teheran and Turkestan, while the paper by MANGIN reviewed above records its occurrence in Aleppo.

C. M. W.

WOLFF. **Dermal Leishmaniasis in Surinam.**—*British Guiana Med. Annual for 1923.* pp. 19–20. [4 refs.]

A note on Forest Yaws in Surinam—an account of the earlier work of FLU and BONNE.

C. M. W.

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Olivier (J.). **Notes sur la fièvre récurrente.**— *Ann. Soc. Belge de Méd. Trop.* 1924. Jan. Vol. 3. No. 3. pp. 365–376.

This paper gives an account of the author's experiences in the treatment of relapsing fever during an outbreak at Usumbura in the Belgian Congo during 1921–1922. After a number of cases had been treated with 914 a dose of 45 to 60 centigrams was administered as a routine every five days till 7 or 8 doses had been given. The cases which were treated at the commencement of the illness responded best, but there were some on which the drug failed to produce any marked impression. A local rumour credited petroleum with specific powers in relapsing fever, but the author's experiments with this remedy proved it to be quite inefficacious. As regards immunity, it was found that this could not be regarded as absolute after recovery, as 4 cases were encountered in which there was every reason to believe that an attack 6 months after recovery was due to reinfection.

C. M. Wenyon.

Russell (A. J. H.), Ayyar (Adisesha) & Ubhaya. **Epidemiological Observations on an Epidemic of Relapsing Fever in Madras Presidency.**— *Indian Jl. Med. Res.* 1924. Jan. Vol. 11. No. 3. pp. 791–806. With 2 charts & 1 map.

It has generally been supposed that the Madras Presidency has been free from relapsing fever, but the supposed immunity of this part of India is shown to be fallacious, for the authors have studied outbreaks which occurred during 1921–1923 in the Mysore State and other parts of the Presidency. The disease, as elsewhere in India, is one of the cooler months. It was most prevalent in the fertile regions amongst the agricultural labourers, and there was every reason to suppose that it was louse-borne.

C. M. W.

Gregory (Arthur). **Chirurgische Erkrankungen als Komplikation nach Typhus exanthematicus und recurrens.** [Surgical Affections complicating Typhus and Relapsing Fever.]—*Deut. Ztschr. f. Chirurg.* Leipzig. 1923. Aug. Vol. 181. No. 1/2. pp. 66–73.

During the three years following 1919 Russia was ravaged by an unprecedented epidemic of relapsing and typhus fever. It is estimated that during 1920 as many as six million people suffered from typhus alone. While surgical complications were recognised before this the enormous incidence of these diseases during the epidemic gave surgeons a unique opportunity of studying them. During the 3 years 1920, 1921 and 1922 the author had under his personal observation 4,096, 970 and 2,171 cases of typhus fever and 203, 1,124 and 1,376 cases of relapsing fever. In the series of typhus cases the percentage showing surgical complications were 15·8, 10 and 4 respectively, while the relapsing fever series gave percentages of 3·4, 3·4 and 1·1.

The most common complication was suppuration of the subcutaneous tissue giving rise to abscesses. In the series of typhus cases the percentages showing this complication were 4·5, 3·7 and 1·2, the

relapsing fever cases giving percentages of 2·1 and 0·8. These abscesses were generally difficult to cure. They lasted at least one month, often two or more months, and not infrequently led to fistulous conditions. Pyaemia occurred in 17 out of 7,237 cases of typhus fever and was only seen once in a relapsing fever case. Actual abscess of the skin was only seen in 5 of the 7,237 typhus cases. Furunculosis occurred in 23 of the typhus cases and carbuncle in 2. Suppurative lymphadenitis occurred in 0·3 per cent. of typhus and relapsing fever cases. Parotitis complicated 1·7 per cent. of the typhus cases and 0·2 per cent. of the relapsing fever cases. Purulent thyroiditis was noted in 4 of the typhus cases. Gangrene occurred in 82 typhus cases and in 3 relapsing fever cases. The gangrene affected the lower extremities most commonly, but occurred also in the skin of the gluteal region and cheek, the scrotum and penis, the skin and subcutaneous tissues in the form of decubitus acutus, the intestine and elsewhere. The gangrene appeared to result from thrombosis, and in the case of gangrene of the feet the operation of ligature of the popliteal vein seemed to give good results. Other complications noted were laryngitis necessitating tracheotomy, spondylitis, osteoperiostitis and osteomyelitis, arthritis, cystitis, orchitis, phlebitis with thrombosis, otitis and finally erysipelas, which was particularly common in typhus cases during 1920.

C. M. W.

Weissenberg (S.). **Ueber den Einfluss des Fleck- und Rückfallfiebers auf die Menstruation, Schwangerschaft, Geburt und Laktation.**—[The Effects of Typhus and Relapsing Fever on Menstruation, Pregnancy, Parturition and Lactation.]—*Zentralblatt f. Gynäkologie.* Leipzig. 1923. June 9. Vol. 47. No. 23. pp. 904–920.

The conclusions arrived at are as follows :—

1. Neither of these infections is the cause of any gynaecological disease and they leave the endometrium intact. While menstruation during illness and subsequently is continued normally, on rare occasions there is uterine haemorrhage, especially in the case of relapsing fever. In about one third of the cases transitory amenorrhoea is noted.

2. The febrile condition appears to have a purifying influence on the generative organs, as a result of which rapid conception occurs.

3. Pregnancy is often interrupted, the danger being especially noticeable in the case of relapsing fever. Abortion usually occurs in the first month. In the middle period it is less common, but towards the end it is again more frequent.

4. The onset of miscarriage is due to various causes, the final one always being found in the bacterial toxins or the ptomaines from the dead foetus, which act either directly or indirectly by influencing the internal secretions which stimulate the nerve centres.

5. During the early months uterine haemorrhage, which leads to detachment of the membranes and consequent death of the foetus, is the cause of miscarriage. In the later months it is never due to primary death of the foetus but rather to the premature onset of labour, a factor which may sometimes play a part during the early months.

6. This factor is also responsible for the cases of missed abortion.

7. Miscarriage and premature labour show no abnormalities; there is no extension of convalescence and no irregularities in lactation.

8. Pregnancy in itself does not influence adversely the course of typhus fever, a fact which also applies to the actual labour. Prognosis is good and the mortality low.

9. The nearer full term the more frequent are the chances of living children which survive.

10. The height of the temperature as also the severity of the disease bear no relation to the processes of menstruation, pregnancy and labour.

C. M. W.

KUDICKE (R.), FELDT (A.) & COLLIER (W. A.). **Untersuchungen ueber die Spirochäten aus Blut und Liquor von Recurrenskranken und ueber die Heilungsvorgänge beim Recurrens.** [The Spirochaetes from Blood and Cerebrospinal Fluid of Relapsing Fever Cases.] —*Ztschr. f. Hyg. u. Infektionskr.* 1924. Apr. 7. Vol. 102. No. 1/2. pp. 135–154. [33 refs.]

The chief conclusions arrived at as a result of the investigations described in this paper are as follows, the spirochaetes being isolated from human beings by the inoculation of mice.

1. Relapsing fever spirochaetes from an old laboratory strain, and those isolated during an afebrile interval from human beings inoculated with this strain may or may not differ from one another as regards their antigenic properties.

2. Strains of spirochaetes recovered from human beings during the intervals by inoculation into mice differ from one another and from the original mouse strain as regards their antigenic properties.

3. In their subsequent passage through mice these various strains gradually lose their differences.

4. Strains isolated during the second half of an interval may resemble those which appear at the following attack, while those isolated during the beginning of the interval differ from those present at the previous attack.

5. Strains isolated from the cerebrospinal fluid at different stages of the disease may differ from one another.

6. Strains simultaneously isolated from the blood and cerebrospinal fluid of a case almost always differ from one another.

7. The differences appear to be due to the antibodies which appear in the blood, one of which at least has a lytic action on the spirochaetes. Such antibodies are demonstrable also in the cerebrospinal fluid.

8. Whether these antibodies are alone responsible for the diminution in the number of spirochaetes which occurs at the crisis future investigations alone will show.

9. During the attack and especially during the crisis there are developed substances which cannot be regarded as specific, as they affect trypanosomes as well as spirochaetes.

10. It is possible to produce a superimposed infection during the interval in spite of the fact that the first infection is still in existence.

C. M. W.

DE BUEN (Sadi), RODRIGUEZ (Rafael) & CASA (Urbano). [**La fièvre récurrente dans la Province de Caceres (Espagne).**]—*Arch. de Cardiol. y Hematologia.* 1923. Sept. Vol. 4. No. 9. p. 316. [Summarized in *Bull. Office Internat. d'Hyg. Publique.* 1924. Feb. Vol. 16. No. 2. pp. 208–209.]

A record of 5 cases of relapsing fever in Spain, where the disease appears to be endemic. Owing to the unhygienic conditions under which the inhabitants live there is danger of extension of the outbreak, which at present is only of slight importance.

C. M. W.

VAN HOOF (L.). **Conservation du pouvoir infectieux de l'*Ornithodorus moubata* nourri sur reptiles et sauriens.**—*Bull. Soc Path. Exot.* 1924. May 14. Vol. 17. No. 5. pp. 376–378. [2 refs.]

The tick *Ornithodorus moubata* will feed on chameleons and small snakes. Ticks kept in this manner do not thrive very well, there being a high mortality rate. Nevertheless, the author was able to demonstrate that though nourished in this way they continued to remain infective as regards *Spironema duttoni*. The reptile blood did not appear to stamp out the infection in the ticks, which was handed on to the subsequent generation as normally occurs.

C. M. W.

INGRAM (A.). *Ornithodorus moubata*, **Murray, in Relation to Relapsing Fever in the Gold Coast.**—*Ann. Trop. Med. & Parasit.* 1924. Apr. 30. Vol. 18. No. 1. pp. 95–97. [2 refs.]

An epidemic of relapsing fever in the Gold Coast was not dependent upon *Ornithodorus moubata*, which appears to be absent from this colony. A number of ticks were, however, secured from elsewhere and experimental transmission of the spirochaete was attempted without success by feeding the ticks on infected and healthy pouched rats. A number of ticks which had fed on an infected pouched rat were also sent to the Liverpool School of Tropical Medicine, where they failed to produce infection in two rabbits and a monkey. It would appear that *Ornithodorus moubata* is not an efficient carrier of the spironema which caused the recent outbreak of relapsing fever in the Gold Coast.

C. M. W.

SINTON (J. A.). **A Clinical Method for the Cultivation of the Parasite of Indian Relapsing Fever** (*Spirochaeta carteri*).—*Indian Jl. Med. Res.* 1924. Jan. Vol. 11. No. 3. pp. 825–828. With 1 plate. [7 refs.]

The author has applied the method devised by him for the cultivation of the malarial parasite to that of the spirochaete of relapsing fever (see this *Bulletin*, Vol. 19, p. 868). The organism was cultivated from two cases. In one case hydrocele fluid was used, to every 100 cc. of which 1·5 cc. of a 50 per cent. glucose solution was added. In the other, horse serum was used in place of the hydrocele fluid. The blood was taken by the method devised for the culture of malarial parasites, and after inoculation the tubes were incubated at 37° C. In both tubes agglomerated masses of spirochaetes appeared, and as

the organisms in the original blood were not more than one in every seven fields, it was evident that active multiplication had taken place. In the case of the second culture, numerous active spirochaetes were present six weeks after inoculation of the tube, which after a week's incubation at 37° C. had been kept at laboratory temperature.

C. M. W.

D'Avigny (G. Prudot). **Evolution de la formule leucocytaire chez les malades atteints de récurrente au cours d'une épidémie (Soudan 1923).**—*Bull. Soc. Path. Exot.* 1924. Feb. 13. Vol. 17. No. 2. pp. 115–119. With 2 charts.

A study of the blood during an epidemic of relapsing fever among Senegalese troops showed that the number of polynuclear leucocytes at the commencement of the disease was slightly below normal. There was a progressive diminution in their number up to the crisis, when there was an increase which reached a maximum above normal just as the relapse was about to occur. During convalescence there was a gradual return to normal. The changes in the number of large mononuclears was more marked. They remain above normal from the commencement of an attack, increasing in number to a maximum which is reached just before the crisis. During the interval they decrease in number, reaching the normal or slightly below it just before the relapse. As regards the lymphocytes a similar change is noted. These results agree with the statements of other observers. From the point of view of diagnosis the blood picture at the commencement of the disease is of little value unless reliance can be placed in a diminution in the eosinophiles.

The changes undergone by the mononuclears may be looked upon as an indication of the course the disease may be expected to take.

C. M. W.

Trolli (G.). **Un cas de fièvre récurrente traité par le novarsénobenzol Billon. Ictère toxique.**—*Ann. Soc. Belge de Méd. Trop.* Brussels. 1924. Jan. Vol. 3. No. 3. pp. 209–212.

A case of relapsing fever was treated with novarsenobenzol. Two doses of 0·3 and 0·4 gram were administered with no untoward reaction, but when a third dose was given there was a febrile reaction associated with tachycardia, neuritis of the circumflex nerves, erythematous eruption and intense jaundice. Spirochaetes were absent from the blood and they did not reappear later. The author considers this to be a case of intoxication due to the drug, such as other observers have noted in the treatment of syphilis.

C. M. W.

Ławrynowicz (A.) & Alisow (P.). **W sprawie bakterjologji powikłań lasecznikowych (przewaznie paratyfusowych) duru powrotnego. Ein Beitrag zur Bakteriologie der bacillären Komplikationen des Rückfallfiebers.**—*Medycyna Doświadczalna i Społeczna.* Warsaw. 1923. Oct.-Nov.-Dec. Vol. 1. No. 5–6–7. pp. 360–377. German summary pp. 376–377. [21 refs.]

Various authors have recorded the isolation from the lesions of septic conditions which occur as complications of relapsing fever,

of bacilli which resemble those of the paratyphoid group. The view has been advanced that this is a specific organism, but an investigation of 66 strains leads the authors of this paper to the conviction that they are really various inhabitants of the intestine which have found their way into the tissues. Though they may add to the severity of the disease, they cannot be regarded as one specific organism.

C. M. W.

SAGEL. **Zur Behandlung der Dementia paralytica mit Recurrens Duttoni.** [Treatment of G.P. with *S. duttoni*.]—*Muench. Med. Woch.* 1924. Mar. 21. Vol. 71. No. 12. pp. 369–370.

The author gives his experiences in the treatment of 72 G.P.I. cases with relapsing fever. He discusses the course of the superimposed infection in detail and the changes which took place in the nervous symptoms of the patients. He is in agreement with PLAUT and STEINER and with MUHLENS and KIRSCHBAUM that this method of treating general paralysis has its value, but that one must not expect too much. Nevertheless, the course of the disease is favourably influenced in various ways. For the treatment of the cases relapsing fever is less dangerous than malaria.

C. M. W.

PONS (R.). **Notes sur la spirochétose bronchique.**—*Bull. Soc. Path. Exot.* 1924. Feb. 13. Vol. 17. No. 2. pp. 170–179. [37 refs.]

In this paper the author has examined the various records of bronchial spirochaetosis and has come to the conclusion that it is impossible to recognise such a disease clinically, basing his remarks on observations which he has made in Saigon. He refrains from describing the symptoms of his 9 cases of this so-called disease, for fear of adding to the existing confusion, if this is possible.

He commences by pointing out that the condition, supposed at one time to be limited to the tropics, has now been met with wherever it has been looked for. In Saigon the systematic examination of the buccal mucus of healthy individuals shows that they may be divided into two classes. In eight out of every 10 persons the spirochaetal flora of the mouth is scanty; in the remainder spirochaetes are numerous. Dental caries certainly favours their presence. It is worthy of note that the 9 cases of bronchial spirochaetosis studied, all belonged to the second category with a rich buccal flora. In the mouth the spirochaetes are distributed generally and may be recovered from any part of the buccal cavity. The question arises as to where this infection may spread. An autopsy which the author had an opportunity of performing has helped to throw light on this matter. A patient who said he had expectorated blood-stained mucus came into hospital and was actually found to be coughing up small quantities of mucopurulent sputum. There were certain lung signs which led to a diagnosis of phthisis, but no tubercle bacilli could be discovered. The sputum, even after washing out the mouth, contained numerous polymorphic spirochaetes—3 to 10 per field. The buccal flora was also very rich. The patient died of aortic disease. At post mortem there was a complete absence of any pleuro-bronchial lesions. At the

origin of the bronchi there was a slight submucosal sanguineous effusion. Smears were made from all parts of the bronchi and these revealed the fact that the spirochaetes were numerous near the mouth, were less numerous in the larynx, still less at the middle part of the trachea and very scanty at the origin of the bronchi. Below this, in spite of the examination of numerous films, no spirochaetes could be found. It appeared logical to the author to conclude that the spirochaetes discovered in the sputum before death were those discovered at post mortem and that they were identical with those which occurred in the mouth. This lends support to the view expressed by TROCELLO that the oral spirochaetes could extend to the bronchi.

Testing the effect of oral lavage on the spirochaetal flora it was found that this had little effect in reducing their numbers in the parts which would be most easily reached, and that it had no effect on the numbers in more inaccessible recesses.

Considering the statements that have been made as to the individuality of the bronchial spirochaete and its distinguishing morphological characters, and comparing them with his own observations, the author was driven to the conclusion that it is practically impossible to differentiate *S. buccalis* from *S. bronchialis*. Such statements as those which affirm that the oral forms are less motile and retain their motility longer than those from the bronchi and do not produce the coccoid bodies to the same extent could not be verified except in the case of the rapid loss of motility of the bronchial spirochaetes. An attempt was made to differentiate the two forms by means of the index suggested by de MELLO (this *Bulletin*, Vol. 20, p. 137), but discordant results were alone obtained. Fusiform bacilli were always found in association with the spirochaetes, though sometimes they were present in very small numbers. Lavage of the buccal cavity by an antiseptic does not eliminate the possibility of spirochaetes contaminating sputum which is coughed up, and under certain conditions and quite apart from any specific pathogenic action the buccal flora may extend to the larynx and trachea.

When an attempt was made to obtain from the literature describing this condition the clinical picture of the disease, the author realised that polymorphism, if not the greatest confusion, appeared to be the dominating clinical characteristic. It was then that the author saw that to give the symptoms of his 9 cases would be merely adding to the existing chaos. Though several authors claim to have observed cases resulting from contagion, nothing of the kind was associated with the 9 cases studied, nearly all of which were in individuals who were living in close association with others who were free from the condition.

Attempts to reproduce the disease by intratracheal inoculation of rabbits failed.

On the subject of treatment the author points out that the supposed spirochaetal etiology of the condition fixed attention on the arsenicals. He could obtain no evidence that these had any real influence on the infection; on the contrary, a case which was being treated with arsenicals for syphilis developed the condition during the course of treatment.

The author sums up by stating that a disease is determined by certain cardinal features which allow of a diagnosis from the point of view of etiology, epidemiology, symptomatology and therapy. In the case of bronchial spirochaetosis the diagnosis depends solely on the discovery

of spirochaetes, which is subject to numerous errors, while the spirochaetes themselves are lacking in individual characters. Clinical examination cannot identify the condition. Furthermore, there is no proof yet available of the pathogenicity of the spirochaete, which is merely an indication of an affection or group of affections. It appears possible that the spirochaetes merely develop in those localities in which conditions favourable to their growth occur. A case is mentioned of a man with tuberculosis who later developed a spirochaetal infection of the respiratory tract, as evidenced by the appearance in the sputum of these organisms which were specially numerous in the blood-stained portions. This patient had a heavy oral infection, and it appears that the abnormal condition set up by the tubercle bacilli afforded an opportunity for the oral spirochaetes to spread to the air passages. With recovery and disappearance of blood from the sputum the spirochaetes disappeared also. The author does not believe, however, that the spirochaetes are purely saprophytes. He rather thinks that they afford evidence of an abnormal condition due to varying causes and that they are able to give to these conditions characters such as chronicity and ulceration which one is accustomed to associate with the occurrence of spirochaetes in a lesion. [This view appears to be similar to that of DELAMARE on intestinal spirochaetosis (see paper reviewed below).]

C. M. W.

DE MELLO (Froilano). **Identificação morfologica do** *Spirochaeta bronchialis* **Cast. e sua diferénciação dos espiroquetas das arcadas alveolo-dentarias.**—*Bol. Geral Med. e Farmacia.* Bastora. 1924. Feb. 9th Ser. No. 2. pp. 46–59. [8 refs.]

This paper appears to be a continuation of one previously published (this *Bulletin*, Vol. 20, p. 137). The assertion is again made that it is possible to distinguish the bronchial spirochaetes from those of the mouth, and the index mentioned in the previous paper is again employed as a means of differentiating the organism. [In the paper by PONS reviewed above the author made an attempt to test the value of this index, but obtaining discordant results he had to abandon it.]

C. M. W.

DELAMARE (G.). **Divisions transversales et longitudinales chez** *Spirochaeta vincenti* **(variété** *bronchialis*).—*C.R. Soc. Biol.* 1924. Mar. 14. Vol. 90. No. 9. pp. 611–612.

The author has studied the spirochaetes of the bronchi in stained films and believes he has demonstrated multiplication by longitudinal as well as by transverse division. The two processes as he has observed them are described in the paper.

C. M. W.

DE MELLO (Froilano). **Deux nouveaux cas de spirochétose broncho-pulmonaire.**—*Bol. Ger. Med. e Farmacia.* Bastora. 1924. Jan. 9th Ser. No. 1. pp. 7–10. [5 refs.]

A record of two cases of spirochaetal bronchitis from Angola.

C. M. W.

KOUWENAAR (Willem). **Spirochaetosis febrilis, een in de tropen voorkomende kortdurende koorts.** [Spirochaetosis febrilis, a Tropical Fever of Short Duration.] [M.D. Thesis, Amsterdam.]—pp. xi + 176. With 33 charts in text. [61 refs.] 1924. Amsterdam: S. L. van Looy.

Kouwenaar in Deli (Sumatra) distinguishes two types of this fever of 5–7 days, both caused by *Leptospira pyrogenes* Vervoort 1922, a Leptospira of the usual type 0·25 × 10–14 μ, the ends curved and with 24 minute spires, and pathogenic for guineapigs.

The spirochaetosis simplex (58 cases examined), without icterus and never ending fatally, shows various types of fever; the "saddle-back" type is common, but other types (3–days fever; interrupted fever with relapse of 2 days on the 5th or 6th day; continuous; intermittent; irregular; fever with a relapse after 3–5 days; or an insignificant fever hardly ever surpassing 38° C.) are likewise to be found. The fever differs from dengue by its irregularity and the prevalence of a short relapse 3–5 days after the end of the principal fever: it lasts longer than papataci fever and, on the whole, resembles most the Japanese "Nanukayami." A skin eruption is seen on the 4th–6th day in 9 per cent. of the cases. Leucocytosis is usual, accompanied by a shifting to the left of the Arneth scheme, often also by lymphopenia; after the fever is over the normal number of leucocytes is re-established, so is the normal Arneth scheme, but there is a temporary lymphocytosis. The resistance of the red blood corpuscles is normal (*i.e.*, haemolysis in 0·35–0·45 per cent. salt solution). Haemorrhages (nasal) are rare; glandular swellings frequent. Urobilin is always present in urine, bilirubin never; febrile albuminuria and nephritis are frequent.

The spirochaetosis febrilis with icterus (31 cases with 6 deaths) shows the same symptoms as the simple type but more intensely. The exanthem, if present, made its appearance on the 6th–12th day; haemorrhages (nasal, dermal, gingival) were more frequent, as were the relapses of the fever after 3–5 days. The resistance of the red blood corpuscles was heightened during the period of icterus (haemolysis at 0·28–0·35 per cent. saline); during leucocytosis lymphopenia was not well marked. Bilirubin was always present in the urine. Post mortem examination showed icterus; haemorrhages; degeneration and focal inflammation of the liver; heightened phagocytal and haemolytic action of the reticulo-endothelial system (liver, spleen, lymphatic glands); degeneration of muscles of the heart, sometimes with myocarditis; inflammation of the walls of dermal capillaries; bronchitis and pneumonia. The leptospirae were found in the kidneys, liver, spleen, mesenteric glands, heart-muscles; not in suprarenal glands, skin and lungs.

In both types the leptospirae are to be found in the blood (by culture-methods) till the 6th–10th day, in the urine (by culture or direct examination) after the 5th or 6th day. Guineapigs could be infected with the urine, not with the blood. But in the case of the leptospirae from a simple spirochaetosis the strain lost its virulence after the 3rd passage, whereas leptospirae from icterus cases conserved their virulence after the 5th passage.

The incidence (both types taken together) is rather high (*e.g.*, 42 cases among a coolie population of 1,200 within one month), the months December-January and July yielding the highest figures.

Epidemics composed of the simple type only were not infrequent, but the icterus type never occurred alone.

It is concluded that these fevers cannot be identified with dengue, papataci and "Mossman" fever; that some of them, but not all, are very much like Weil's fever and that the simplex cases resemble most nanukayami. It is left undecided whether the two types represent two distinct diseases or whether they are nothing but a mitigated and a grave variety of one and the same disease.

N. H. Swellengrebel.

DELAMARE (G.). **Diagnostic microscopique et valeur sémiotique des grandes décharges de spirochètes fécaux.**—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1924. May 22. Year 40. 3rd Ser. Vol. 48. No. 17. pp. 725–729.

The fact that in perfectly healthy persons spirochaetes may be found in small numbers in the faeces and that in others suffering from some form of colitis enormous numbers may be found has led the author to enquire as to the limits of the intensity of infection which indicate the border line between health and disease. He thinks that 6 to 10 spirochaetes per field (presumably of the 1/12 objective) is the standard to adopt. It seems to him probable that as the spirochaetes are found to be numerous in such a variety of different conditions it is impossible to attribute any particular disease to their presence. It appears as if they multiply rapidly when the intestine is in a condition favourable to their growth. Their frequency in such conditions as cholera and amoebic infections is a case in point. Without attributing to the spirochaetes any pathogenic properties, their presence in large numbers is nevertheless an indication that the intestine and especially the colon is in an abnormal condition. And when the symptoms of that condition, or other reasons, suggest a possibility of cholera or amoebiasis the discovery of spirochaetes in the faeces alone should be taken as an indication that further examination for the specific organism may be successful. [The views expressed in this paper are similar to the conclusions arrived at by PONS above, in connexion with bronchial spirochaetosis.]

C. M. W.

v. ANGERER (Karl). **Filtrationsversuche mit Wasserspirochäten.** [Filtration Experiments with Water Spirochaetes.]—*Arch. f. Hyg.* 1924. Vol. 92. No. 7. pp. 325–328.

Owing to the conflicting statements that have been made as to the possibility of water spirochaetes being able to pass through a Berkefeld candle, the author repeated the experiment. He found that such a passage was possible but that it depended on the pressure. With the lowest possible pressure the spirochaetes did not pass through. When colloids were present in the medium the passage was hindered to a greater extent than by lowering the pressure. Young cultures yielded spirochaetes which passed through more easily than those of old cultures. It is essentially the living spirochaetes which can make their way through the filter. The filtrates were controlled by direct examination and by culture and no evidence was obtained of the existence of any granule or invisible stage of the organisms.

C. M. W.

PONS (R.). **Sur l'existence, dans les liquides souillés de sang, de filaments, non organisés, pouvant être confondus avec des spirochètes.**—*Bull. Soc. Path. Exot.* 1924. Apr. 9. Vol. 17. No. 4. pp. 307–309. With 1 fig. [1 ref.]

Attention is called to the filaments which can be observed in fluids contaminated with blood and might be confused with spirochaetes. They originate from the stroma of the red cells and are of two types. The one type is a short filament 8–10 microns in length and 0·2–0·3 microns in breadth. The ends appear to be slightly swollen and more refractile than other parts of the filament, which itself is made up of a series of particles. Though exhibiting Brownian movements they do not progress when observed in relation to other particles in the fluid. The other type is a long filament 8–20 microns in length. It is finer than the filament of the first type and may reach the limit of visibility in this respect. It appears to have the form of a ribbon and, like the others, has a refractile granule at each extremity. No movement of progression could be observed in them. Unlike true spirochaetes, they cannot be satisfactorily stained, so that confusion with spirochaetes ought not to occur. [Attention was called to these filaments, which were shown in an illustration, in this *Bulletin*, Vol. 21, p. 282.]

C. M. W.

CHAPUT (P.). **Les arsenicaux employés dans le traitement des affections spirillaires.**—*Arch. Méd. et Pharm. Milit.* 1923. Oct. Vol. 79. No. 4. pp. 501–531. [11 refs.]

In this paper an account is given of the chemistry and interrelationships of the chief organic compounds of arsenic used in medicine. Beginning with BECHAMP'S discovery of atoxyl in 1860–1863, the author shows that little progress was made until EHRLICH and BERTHEIM in 1907 discovered the real nature of this substance, and by revealing the presence in it of an unaltered amino-group made atoxyl the parent of practically all the synthetic arsenical drugs of the present day.

EHRLICH'S hypothesis that aromatic arsinic acids, such as atoxyl, only became spirillicidal on reduction in the body to trivalent arsenic compounds led to the researches which produced the arsenobenzenes (salvarsan, neosalvarsan, etc.), but, in conjunction with EHRLICH and HATA'S observation that these pentavalent arsenic compounds gave rise to nervous troubles, it had also the effect of diverting attention from the simpler derivatives allied to atoxyl, until FOURNEAU and other workers in France reverted to this line of work in the last few years, and have shown that some of these compounds, *e.g.* the hydroxyaminophenylarsinic acids, may prove to be useful spirillicides.

Full justice is done to this and other French work on this subject, but in the account of the arsenobenzenes no mention is made of the important work done in this country by FARGHER and PYMAN and later by KING on the accessory constituents of commercial salvarsan, nor to the American work on the same subject, and in the very condensed account of the so-called " metallic derivatives of salvarsan " no mention is made of the considerable body of evidence brought forward by GRAY in this country and by other workers in Germany and the United States that silver salvarsan, the best known of these supposed co-ordination compounds of salvarsan, is merely a mixture of sodium salvarsan and colloidal silver.

T. A. Henry.

RAT BITE FEVER.

ONORATO (Raffaele). **Il sodòku in Tripolitania.**— *Arch. Ital. Sci. Med. Colon. Tripoli.* 1923. May, June, July-Aug.-Sept., & Oct.-Nov.-Dec. Vol. 4. Nos. 5, 6, 7-8-9, & 10-11-12. pp. 156–159; 162–191; 193–218; & 221–238. [52 refs.]

Having under his care in Tripoli a woman and her child who were both suffering from rat bite fever, the author conducted a long series of investigations involving a search for the organism in the two cases, inoculation of animals and the culture of the organism from the cases and the experimental animals. In both cases, as well as in the inoculated animals and in the culture, there were present organisms of two types. The one corresponded to the small one usually associated with the disease, while the other resembled a leptospira. Attempts were made to separate these but without avail, so that the author is finally driven to the conclusion that the causative agent of rat bite fever is a polymorphic organism and that both types are merely different developmental stages of one and the same organism. [It seems possible that the second type, which is said to be 8–9 microns in length, with movements which are undulating rather than spiral-like, might be merely blood filaments. The author does not mention the filaments themselves, and as he does not appear to have observed any connecting links between the two types of organism described it is conceivable that he was mistaking filaments for leptospira-like organisms. Even if this explanation is correct it does not invalidate the results of his work, for the leptospira-like structures are always associated with the short organism, which is certainly a definite parasite.]

The chief interest of the work lies in the successful culture of the organism, which has been attempted without success by many observers since the announcement of a method of cultivating it by FUTAKI and his collaborators in 1917 (this *Bulletin*, Vol. 13, p. 338). Two media were employed. The first was that of SHIMAMINE. It was prepared by dissolving by shaking 0·5–0·75gm. of nucleinate of soda in 100 cc. of horse serum and then passing through it for 3 or 4 minutes a current of anhydrous carbonic acid gas. The medium is then heated to 60°C. for an hour on 3 consecutive days and finally for half-an-hour at 65°C. on the 4th day. The medium, which is then ready for inoculation, consists of a solid and a liquid part. The other medium employed was what the author calls haemolysed rabbit serum medium. He does not give the details of its method of preparation. The organism grows at 25°–26°C. and is a facultative anaerobe. Many of his cultures were made aerobically, but under these conditions the growth is less intense and less regular. In both cases search for the organism in the urine, sweat, cerebrospinal fluid, blood, skin at site of eruption and lymphatic gland was made by direct microscopic examination of stained films and by dark ground illumination of moist films, by inoculation of animals and by culture. In both cases the blood gave a positive result by all these methods, while in one case the organism was isolated from the skin by the inoculation of an animal and in the other from a lymphatic gland by the same method.

Of the infected animals a detailed examination of a large number was made. In most cases both by the culture method and by the inoculation of other animals the organism was recovered from the blood, cerebrospinal fluid, urine, lymphatic gland and various internal organs.

In many cases it was discovered in these situations by direct examination of stained smears or by dark ground illumination. The constancy with which the author obtained positive culture from these animals indicates that he has used a reliable method for cultivating the organisms. The details of the numerous experiments and observations in the two cases and in the experimental animals are arranged in four elaborate tables. In addition to the experimental work outlined above the paper gives a careful description of the two cases, the course of the temperature being illustrated by two instructive charts. Furthermore, the author gives a very good review of most of the previous work and observations on this disease, failing, however, to mention the work of Row in India. Apart from the successful culture work the paper contains little new information.

C. M. Wenyon.

Dujarric de la Rivière (M. R.). **Contribution à l'étude des spirochétoses. Le sodoku.**— *Ann. de Méd.* 1918. Mar.–Apr. Vol. 5. No. 2. pp. 184–205. With 3 figs. & 4 charts in text. [59 refs.]

This is a critical review which does not pretend to give any new information on rat bite fever. Dealing with the nomenclature of the causative organism the author points out that the name *Spirochaeta morsus muris* given to it by Futaki, Takaki, Taniguchi and Osumi in 1916 cannot stand, as, being trinomial, it does not conform to the rules of nomenclature. He therefore proposes the name *Spirochaeta japonica*. As regards the similar organisms which have been found in rodents, though they are morphologically indistinguishable from the one causing rat bite fever he is of the opinion that they cannot be identified with it as they are not pathogenic to the same extent. He is of opinion that *S. laverani* Breinl and Kinghorn, 1906, *S. muris* Wenyon, 1906, *S. muris* var. *virginiana* MacNeal, 1907 and *S. muris* var. *galatziana* Mezinescu, 1909, are all identical with the form described by Carter in 1887 as *Spirillum minor*.

C. M. W.

O'Leary (Paul A.). **The Dermatologic Aspects of Rat-Bite Fever.**— *Arch. Dermat. & Syph.* 1924. Mar. Vol. 9. No. 3. pp. 293–304. With 6 figs. [20 refs.]

The paper describes two cases of rat bite fever in America. From neither was the causative organism isolated, but response to arsenical treatment was immediate. The cases appeared to be typical and the skin eruption, which is well illustrated in a series of photographs, conformed in practically every detail to the published accounts. It is erroneously stated that so far only Japanese observers have been successful in isolating the organism.

C. M. W.

Row (R.). **On the Rat-Bite Spirochaete.**— *Indian Jl. Med. Res.* 1924. Apr. Vol. 11. No. 4. pp. 1283–1284. [6 refs.]

Reference is made to a paper by Parmanand (this *Bulletin*, Vol. 20, p. 881). The author states that in this practically all his observations on rat-bite fever in India were confirmed by Parmanand except the claim made by him that he had been able to demonstrate flagella in the

organism. Row thinks that PARMANAND's statement regarding the flagella is still debatable and considers that the question of the identity of the Bombay organism and that of Japan, the crux of which is the presence or absence of flagella, is still *sub judice*.

C. M. W.

MOOSER (H.). **Experimental Studies with a Spiral Organism found in a Wild Rat.**—*Jl. Experim. Med.* 1924. Apr. 1. Vol. 39. No. 4. pp. 589–602. With 3 plates. [15 refs.]

The author made an experimental study of an organism, which appeared to be that of rat-bite fever, which he discovered in the blood of the rat *Mus decumanus*. It was inoculable to rats and guineapigs, the infection in the latter being fatal. On one occasion a guineapig was infected by the bite of another guineapig which harboured the organism. Eye lesions were found in all the guineapigs, and the organism was found in the discharge from the eyes as well as in the cornea. Similar lesions occurred in most of the rats, and the secretion from the eye in one case was proved to be infectious to a guineapig. The author concludes that the eye lesions are an evident and possibly the only source of the spiral organisms transmitted by biting. He thinks it is possible that Weil's disease may sometimes be accounted for in this manner.

C. M. W.

MATSUMOTO (Shinichi) & ADACHI (Yogoro). [**On the Primary Sclerosis in Rat-Bite Fever of the Rabbit.**]—*Hifuka Kiyo* (*Arch. of Dermat.*). 1923. July. Vol. 1. No. 4. [Summarized in *Japan Med. World.* 1924. Feb. 15. Vol. 4. No. 2. pp. 42–43.]

This is a short note on the results of inoculation of the organism of rat-bite fever into the subcutaneous tissue of the scrotum of the rabbit. There was at first local infiltration and oedema followed by sclerosis and ulceration, and finally cicatrization. The lesions behaved in all respects like those produced by *S. pallida*.

C. M. W.

LAIGNEL-LAVASTINE, BOUTET, SERRANT & ARBEIT. **Un cas typique de Sodoku à Paris.**—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1924. Feb. 7. Year 40. 3rd Ser. Vol. 48. No. 4. pp. 105–109. With 1 chart. [5 refs.]

A typical case of rat-bite fever in Paris. The organism was isolated from the blood by inoculation of mice.

C. M. W.

INFECTIOUS JAUNDICE.

GULLAND (G. Lovell) & BUCHANAN (George). **Spirochaetosis icterohaemorrhagica in East Lothian.**—*Brit. Med. Jl.* 1924. Feb. 23. pp. 313–314. With 4 figs.

An outbreak of Weil's disease occurred amongst the coal miners of East Lothian, the first cases being noted in April or May 1923. The patients have been almost entirely young coal miners employed in different pits, the earlier cases coming from one pit, the later ones from

another. One farm labourer, however, contracted the disease. In all about 18 cases have occurred. The affected pits were wet and rats were numerous. Clinically the cases were typical of the disease, and the organism isolated from the urine of one of the cases and from pit rats showed that both behaved in guinea-pigs like typical *Leptospira icterohaemorrhagiae.*

C. M. Wenyon.

Hoffmann (W. H.). **Die markige Schwellung der Darmfollikel bei der Leptospireninfektion.** [Swelling of the Intestinal Follicles in Leptospira Infection.]—*Muench. Med. Woch.* 1924. Apr. 4. Vol. 71. No. 14. pp. 428–429. With 1 text fig.

The author has noted that in Weil's disease, both in human beings and in experimentally infected animals, there is marked swelling of the lymph follicles of the intestine. It bears a resemblance to that occurring in typhoid fever. Whether this condition occurs only in Weil's disease or will be found in other leptospira infections also, further investigations will show.

C. M. W.

Hieta (Kentaro). [**On the Pathological Changes of the Liver and the Development of Jaundice in Spirochetosis Icterohemorrhagica.**]—*Namman Igakkwai Zassh* (*Jl. of S. Manchurian Med. Soc.*). 1923. Dec. Vol. 12. No. 2. [Summarized in *Japan Med. World.* 1924. Apr. 15. Vol. 4. No. 4. p. 99.]

From a histological examination of the liver from 19 cases of Weil's disease the following changes were noted. Though the liver was not much enlarged the hepatic stroma appeared turbid and the hepatic cells swollen. The cell bundles appeared to be irregular, while the hepatic cells lost their attachments. The nuclei of the cells were swollen, while the chromatin network was obscured and the chromatin dissolved. Every transition between dilated and undilated capillaries was found. The jaundice which occurs in the disease is thought to be due to the separation of the hepatic cells, which permits the bile to enter the blood stream.

C. M. W.

Oda (Toshiwo). [**Experimental Observation on the Acute Insufficient Blood Circulation which is met with in Spirochetosis Icterohemorrhagica.**]—*Tokyo Igakkwai Zasshi* (*Jl. of Tokyo Med. Soc.*). 1923. July. Vol. 37. No. 7. [Summarized in *Japan Med. World.* 1924. Jan. 15. Vol. 4. No. 1. p. 16.]

By noting that the rate of death due to suffocation is more rapid in animals suffering from experimental Weil's disease than in normal animals, the author concludes that the heart function is greatly obstructed in this disease.

C. M. W.

Hoffmann (W. H.). **Estudio clinico de la enfermedad de Weil.**—*Rev. Med. y Cirug. de la Habana.* 1924. Mar. 25. Vol. 29. No. 6. pp. 176–182. [1 ref.]

A short paper on the symptomatology of Weil's disease not adding any new information.

C. M. W.

YELLOW FEVER.

FOWLER (James Kingston). **Yellow Fever in Gibraltar in 1804.**—*Jl. Roy. Army Med. Corps.* 1924. June. Vol. 42. No. 6. pp. 401–413. [2 refs.]

As a result of the examination of a manuscript entitled "Reports Relative to the Diseases of Gibraltar" by W. W. FRASER, Deputy Inspector of Hospitals, the author has come to the conclusion, apparently with ample justification, that a disease introduced into Gibraltar by a smuggler who died on August 10th or 12th 1804 was yellow fever. The disease spread to the civil population and thence to the garrison, which at that time was at a strength of 4,052. The civil population was probably about 9,000. Between the beginning of September, when the epidemic got a hold on the population, and the latter days of December, when it became extinct, there were 5,946 deaths. After the epidemic had ceased only 28 adults could be discovered who had resided within the walls and had escaped the infection. At about the same time the disease appeared at Algeciras with a similar population, but owing to the energetic measures which were taken to combat it the experiences of Gibraltar were averted. Those who wish to consider the evidence on which the conclusions are based must read the entire article, which is a most interesting one. [See also this *Bulletin*, Vol. 15, pp. 286–7.]

C. M. Wenyon.

WANSTROM (Ruth C.). **Occurrence and Staining of *Leptospira icteroides* in Guineapigs inoculated experimentally, with a Study of the Lesion produced.**—*Jl. Infect. Dis.* 1924. Feb. Vol. 34. No. 2. pp. 110–116. With 3 plates. [7 refs.]

In inoculated guineapigs *Leptospira icteroides* occurs in all the tissues, especially where haemorrhagic areas occur. The organisms are found in greatest numbers in the liver, they are numerous in the kidneys and occur to a less extent in the spleen and lung. In other tissues they are more widely scattered. The marked fatty degeneration of the liver and kidney described by NOGUCHI and PERRIN was not noted. There was acute congestion of all the organs. It was most evident in the liver, kidney, spleen, lung and lymph nodes, while the liver and kidney cells revealed cloudy swelling. The heart muscle showed Zenker necrosis. Phagocytosis of leucocytes was fairly marked, while there was slight leucocytosis. The tissue changes were not as definite as in cases of yellow fever and did not differ from those of experimental Weil's disease.

The Warthin-Starry silver-agar stain was found to yield results as satisfactory as those obtained with *S. pallida*.

C. M. W.

NOGUCHI (Hideyo). **The Pfeiffer Reaction in Yellow Fever.**—*Amer. Jl. Trop. Med.* 1924. Mar. Vol. 4. No. 2. pp. 131–138. [8 refs.]

A positive Pfeiffer reaction obtained with the serum of patients recently recovered from a disease suspected of being yellow fever provides confirmatory evidence of the infection. A negative reaction, however, may be obtained with the serum of persons who have had undoubted yellow fever; hence a clinical diagnosis of this disease

cannot be negatived because the reaction fails. The capacity of the serum to give a positive Pfeiffer reaction does not endure for long, so that the reaction gives no indication of the actual immunity which, in the case of genuine infections, persists for the remainder of life.

That *Leptospira icteroides* is the causal agent of yellow fever is borne out by the fact that in Brazil the serum of convalescents from yellow fever gave positive Pfeiffer reactions with strains of the organism isolated in Ecuador, Mexico and Peru, while it gave negative reactions with *L. icterohaemorrhagiae.*

C. M. W.

Rendón (Garcia). [**Procedimiento fácil de hacer el diagnóstico bacteriológico de la fiebre amarilla.**] [An Easy Method of Diagnosing Yellow Fever Bacteriologically.]—*R. Méd. Veracruzana.* [Summarized in *Rev. Española de Med. Cirug.* 1924. Mar. Vol. 7. No. 69. p. 155.]

3 cc. of blood from the suspected patient is inoculated into the peritoneal cavity of a guineapig. If in the course of three days or so the animal's temperature rises above 40° C., the leptospira can be cultivated from its blood. In a positive case the guineapig may die with subnormal temperature, when the "jaundice and all the haemorrhagic lesions described in human cases will be seen." If the patient is dead a portion of the liver and of the kidney should be ground in a mortar with normal saline and 2 cc. of the emulsion inoculated intraperitoneally into a guineapig and the animal observed as before. [The author naïvely adds: "The negative result of these observations does not warrant our rejecting the diagnosis of yellow fever."]

H. Harold Scott.

R. Med. Veracruzana. [**Obtención de los cultivos de Leptospira con el medio de Noguchi.**]—[Summarized in *Rev. Española de Med. Cirug.* 1924. Mar. Vol. 7. No. 69. pp. 155–156.]

To Ringer's solution with 2 per cent. agar melted and brought to 50° C. is added 1–1·5 cc. of sterile rabbit-serum. A few drops of blood taken from the heart of an infected guineapig are inoculated into each tube, the whole covered with 2–3 cc. of sterilized liquid paraffin and incubated at 37° C. In 8–10 days there is a growth of leptospira beneath the paraffin. Animals suspected of being reservoir hosts are caught and killed; portions of the liver, spleen and kidney are emulsified in normal saline and injected into the peritoneal cavity of young guineapigs and these are then kept under observation as described in the paper by Dr. Rendón.

H. Harold Scott.

Fróes (João A. G.). **Etiologia da febre amarella—Contribuçao Brasileira ao esclarecimento desse arduo problema.**—*Brazil Med.* 1924. May 3. Year 38. Vol. 1. No. 18. pp. 245–253.

This paper, the substance of an inaugural address, is only of historical interest and traces the investigations into the etiology of yellow fever which have been conducted in Brazil and the various theories which were advanced to explain it down to the discovery of the leptospira by Noguchi.

C. M. W.

Noguchi (H.). **O leptospira icteroides.**—*Rev. Med.-Cirurg. do Brasil.* 1924. Apr. Vol. 32. No. 4. pp. 171–177.

A letter written to A. G. Fróes in which Noguchi expresses his views on the nature of spirochaetes, especially with reference to *Leptospira icteroides.* The date 1914 is evidently a misprint, as a later date is quoted in the letter.

C. M. W.

SLEEPING SICKNESS.

VASSAL (J.). **Etudes sur la maladie du sommeil (Alima, Likouala, Bas-Oubangui).**—*Bull. Soc. Path. Exot.* 1924. Mar. 12. Vol. 17. No. 3. pp. 234–259. With 1 map.

The data recorded in this paper were accumulated during a tour made by the author extending over a period of two months. He had two hospital assistants and examined more than 13,000 natives. The results of the examination of the population are summarized in the following table :—

Nos.	Division by regions.	Subjects seen.	Number of cases.	Percentage.	Observations.
1	Banks of Congo and Bas-Oubangui ..	867	38	4·3	As well as 300 subjects seen with fifty suspects.
2	Mossaka and territory of Mossaka	1,661	83	4·9	
3	Region of Makona and Likouala Mossaka from N'Dolo ..	2,970	124	4·2	
4	Region of Etoumbi-Ololi Odzala ..	1,360	100	7·3	
5	Basin of Kouillou and Fort-Rousset ..	1,610	38	2·3	
6	Basin of Alima ..	4,822	92	1·9	
	Total ..	13,290	475	3·5	

The author discusses the various means of diagnosis and lays stress on the importance of gland puncture as a means of recognizing cases in the field.

The following conclusions are given :—

1. From 1st December 1922 to 2nd February 1923, in the regions of Likouala Mossaka and Alima, 13,290 natives were examined and 475 (3·5 per cent.) found to be infected with sleeping sickness : the sick were treated with 2 injections of atoxyl.

2. The benefit of prophylactic treatment will be extended all over the country.

3. The methods employed have been controlled and judged efficacious. The diagnosis by gland puncture and microscopic examination, although not applicable to the case of children of tender years, ought to continue to be used generally to the exclusion of all others.

4. The collaboration of public services and the utilization of native hospital assistants will help to meet the difficulty as regards the European staff and to reorganize the sections on a larger scale.

5. Rudiments of medical knowledge will contribute to the progress of hygiene in these countries.

W. Yorke.

HUERTA (Plácido). **Progresos de la tripanosomiasis humana en Fernando Póo.**—*Siglo Med.* 1924. Apr. 12. Year 71. Vol. 73. No. 3670. pp. 367–371.

In Fernando Po in 1909 Dr. PITTALUGA found only 9 cases of trypanosomiasis. Eight years later the author saw more than 80 cases in

the hospital at Santa Isabel, and the number continued to increase during the Great War, many cases occurring amongst the soldiers. Returning in 1920 he found that the number of cases registered at the hospital during the year had risen to 150. In 1923 in a single month (July 15 to Aug. 14) 36 cases were seen. He calculates that of the indigenous population 50 per cent. infection is a low estimate, and that in the island of Santa Isabel alone there are probably about 1,000 cases. There is reason to believe that prior to 1898 trypanosomiasis was rife in Fernando Po, and the paucity of cases between that time and 1917 is ascribed to practical annihilation of the people. Re-establishment of agricultural activity brought in labourers from without. Glossina was present in very large numbers, the animals had constituted reservoir hosts, and the disease again made headway till it attained the high percentage mentioned.

H. Harold Scott.

YAKIMOFF (W. L.). **Sur la question de l'infection de l'homme par les trypanosomes.**—*Ann. Soc. Belge de Méd. Trop.* Brussels. 1924. Jan. Vol. 3. No. 3. p. 307.

At the end of the year 1914, one of the author's collaborators (Mlle. N. A. Z.) accidentally inoculated herself with 1 cc. of citrated blood heavily infected with *T. brucei* [the origin of the strain is not stated]. A week later her blood was inoculated into a mouse which died ten days later without becoming infected. The lady was in poor health during the following two weeks, but there was no rise of temperature and the blood remained negative. Since 1914 she has had typhus, recurrent fever, has been accidentally poisoned with morphia and sublimate, has been pregnant, and has suffered privation during the Civil War, but has presented no sign of trypanosomiasis. The case is contrasted with that of LANFRANCHI, who infected himself accidentally with *T. evansi*.

W. Y.

VANDERYST (Le R. P.). **Les diagnostics empiriques et scientifiques de la trypanose humaine en prophylaxie sociale.**—*Rev. Méd. et d'Hyg. Trop.* 1924. Mar. Vol. 16. No. 3. pp. 65–86. [8 refs.]

As the result of a lengthy discussion of the subject, the author reaches the following conclusions :—

The great anti-trypanosomiasis missions in Africa ought to be organized in a scientific manner.

The search for infected cases ought to be based not only on palpation of the cervical glands, but rather on all the other clinical symptoms which are observed in trypanosomiasis.

Pseudo-diagnosis based exclusively on enlarged cervical glands is without positive value.

Medical diagnosis based on all the clinical symptoms has a more or less great value when the cases suspected can be kept under observation for a long period. It is, however, inadequate as a fundamental method for a scientific mission.

Microscopic diagnosis is the only scientific method for the immediate diagnosis of sleeping sickness.

Every prophylactic mission should be based on this microscopic method of examination and no native should be classified among the infected if the microscopic examination of his blood and gland juice is negative.

W. Y.

BRUMPT (E.). **Le *Trypanosoma rhodesiense*. Faits et hypothèses concernant son individualité.**—*Ann. Parasit. Humaine et Comparée.* 1924. July. Vol. 2. No. 3. pp. 254–273. With 3 text figs. [25 refs.]

In this somewhat lengthy paper the author, after giving a description of the morphology, pathogenicity, transmission and reservoir of *T. rhodesiense*, discusses its relationship to *T. gambiense* and *T. brucei*.

The following are the conclusions :—

1. Recent epidemiological researches show in the author's opinion that *T. rhodesiense* is a good species.

2. The classification of trypanosomes should be based on the summation of their characters, both morphological and biological.

3. The natural immunity of certain species of hosts to natural infection is a character of great value and constitutes in the absence of others an excellent criterion for identifying certain species. It is difficult to admit of the existence of rapid biological transformations of trypanosomes occurring, as it were, before our eyes, in Africa, during the last few years.

4. Mechanical transmission of the trypanosomes parasitic to man in Africa does not explain the gravity of certain epidemics, a gravity which depends in part—as do diseases not transmitted by intermediate hosts—on certain factors which constitute for the ancient authors the "genie epidemique," factors which we are still incapable of determining precisely, and also on the absence of immunity amongst populations newly subjected to infection.

5. Much remains to be studied concerning the epidemiology of sleeping sickness due to *T. rhodesiense* and to *T. gambiense*.

6. It would be interesting to repeat with these organisms the experiments on the geographical variations of virulence and on superinfection which the author has effected with *T. inopinatum* and with the leech *Helobdella algira*.

W. Y.

DAVEY (J. B.). **The Outbreak of Human Trypanosomiasis (*Trypanosoma rhodesiense* Infection) in Mwanza District, Tanganyika Territory.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1924. Feb. 21. Vol. 17. No. 8. pp. 474–481. [4 refs.]

In September and October 1923 the author accompanied by Dr. MACLEAN, the medical officer in charge of the district, spent nearly one month in the Mwanza sleeping sickness area. Since the discovery of the outbreak by MACLEAN early in 1922, about 5,000 persons have been removed from the fly infested forest to fly-free localities and the principal roads cleared to a width of 100–200 yards on either side ; these measures were practically completed in 1922. Cases of the disease and suspects have been isolated and treated in camps in fly-free country.

Davey considers that the disease has been endemic in the area for several years and thinks it extremely unlikely that the case diagnosed on 2 April 1919 was the first. He points out that it is significant that for at least four years a considerable number of cases of sleeping sickness escaped detection within 50 miles of a medical station. It is by no means improbable that sleeping sickness is present in other parts of the country ; the history of the disease in Nyasaland shows that *T. rhodesiense* infection readily escapes observation and it has now been reported from a large part of the fly-infested game areas of that country.

Davey was much impressed with two facts which did not perhaps receive due emphasis in previous accounts [DUKE and SWYNNERTON, *vide* this *Bulletin*, Vol. 20, p. 309 and p. 311].

The first is that villages, in the usual meaning of the term, do not exist. The huts in ones, twos and threes are scattered over wide tracts of country. Each unit of one to three huts comprises a family party, and a number of units scattered over an area of several square miles makes up a village. In open country each unit has its euphorbia enclosure; when, as is often the case, the site of the village is one of the low hills capped with granite boulders, the units are disposed around its base. The abandoned villages visited in the fly area were of this type or consisted of separate units of two or three huts in a small clearing closely surrounded by bush. This segregation system must exercise a very distinct restraining influence on epidemic disease.

Secondly, the author was impressed by the abundance of wild game in the area. In the fly forest or thorn scrub the ground was seamed by the spoor of zebra, antelope, giraffe, etc., and there were everywhere complaints of the great damage done to the gardens by these animals in the wet season. The author suggests that the fact that SWYNNERTON found but little game was due to some quite temporary diminution in the localities visited by him. A pack of wild hunting dogs will scare all game away from a spot, and furthermore, at the time SWYNNERTON visited the area, the rains had not long ceased and hunting in the long grass must have been very difficult. Davey cannot for a moment accept SWYNNERTON'S hypothesis that owing to scarcity of game the fly was driven to feed on man, nor does he consider that the proposed experiment in game destruction has for practical purposes been carried out in the area.

With reference to the effect of the preventive measures adopted, Davey states that in 1922 MACLEAN diagnosed microscopically 42 cases; these include only a few of the 37 diagnosed by DUKE at the sleeping sickness camps. Owing to pressure of work some cases died before MACLEAN examined their blood and in suspected cases treatment was often commenced before awaiting the confirmation of the diagnosis. Probably quite 50, including DUKE'S cases, died before diagnosis was confirmed by MACLEAN. In 1923, after removal of the forest villages to fly-free areas, 40 cases had been diagnosed up to 20 October, and probably there were at least nine other cases whose blood was not examined. It is certain that both in 1922 and 1923 a number of cases were never brought to notice, but probably, for several reasons, more escaped observation in the former year than in the latter. The diminution of the disease produced by removal of the population is not therefore very striking and makes caution necessary in accepting the doctrine of direct mechanical infection.

Information of considerable interest is given regarding the distribution of the cases. The 22 cases in Ntusu were drawn from 16 different villages; three cases came from one village, and two from each of four others; there were two cases from one village in Nunghu Sultanate; the remaining cases originated in separate villages. In no case could infection be definitely attributed to contact with another case, and now that all the villages have been removed from the forest it must be comparatively seldom that opportunity for direct infection by mechanical transmission can arise.

The author was much struck by the fact that large herds of cattle were grazed in what appeared to be dangerous proximity to the

forest; it was said by the sultans that no sickness resulted nor did the author find a single instance of infection by blood examination.

The history of many cases shows that, for some time after infection, it is possible for long journeys to be made by the victim. Following the initial attack of pyrexia, there is frequently a period of 4, 6, or even more weeks when acute symptoms are absent and the patient is able to follow his ordinary pursuits; as the blood is then rich in trypanosomes, it appears that the part played by such persons in infecting the fly may have been underestimated. Davey considers that the progress of the outbreak in Mwanza district throws some light on the question of the relative importance of infected man and game as sources of infection. If infected man is the chief or only culprit, isolation of the cases in fly-free areas should have produced a more striking effect on the course of the outbreak than has been the case. If mechanical transmission only is at work, the effect of this measure should have been almost instantaneous.

Summary and Conclusions.

"1. *Origin of the Outbreak.*—The outbreak was almost certainly in full swing before the famine of 1919–20. It is more probable that infection was derived from game than that it was introduced by invading military units at a later date.

"2. *Method of spread.*—Infection is acquired from the tsetse in the forest. Whatever may have been the case early in 1922, the evidence of 1923 all points to transmission by cyclically infected flies.

"3. *Game and Fly.*—There is ample evidence that game is, and has for years been, comparatively plentiful in the area. The hypotheses are untenable that (i) the fly has been consistently driven to feed on man owing to scarcity of game, and (ii) the oft-demanded experiment in game destruction has been practically carried out in the area.

"4. *Source of infection.*—The probable importance of infected man as a source of infection of the fly in sleeping sickness areas has been underestimated. The relative importance of men and infected game in this respect is problematical.

"5. *Distribution of* T. rhodesiense *infection.*—The outbreak is another link in the chain of evidence that wherever game infected with the *brucei*-type of trypanosome fly of the *morsitans* group and man are brought into sufficiently close contact, cases of human infection will arise; they may escape detection for years.

"6. *Cultivation of the soil* is the only radical preventive of tsetse-fly and trypanosomiasis in Africa. The proximity of numbers of wild game is inimical to cultivation.

"7. *The facts which are known* regarding the Mwanza outbreak do not, in any way, invalidate the general conclusions on *T. rhodesiense* infection of man reached by the Royal Society's Scientific Commission to Nyasaland."

W. Y.

Archivos Brasileiros de Medicina. 1924. Jan. Vol. 14. No. 1. pp. 52–88.—**A doença de Chagas. Parecer da Commisão da Academia Nacional de Medicina, constituida pelos Drs. Alfredo Nascimento, Henrique Duque, A. MacDowell e Moreira da Fonseca, sobre questões referentes á doença de Chagas, lido na sessão de 29 de Novembro de 1923. Informaçôes prestadas pelo Dr. Carlos Chagas á Academia de Medicina.** [Report of the Commission appointed to consider the Question of Chagas's Disease.]

Doubt having been cast upon the work of Dr. Carlos Chagas relative to American trypanosomiasis by certain members of the National

Academy of Medicine of Brazil, some regarding the trypanosome as a harmless accidental blood-parasite, others not only denying the existence of such a condition but impugning the bona fides of Dr. CHAGAS, a Commission was appointed to make enquiries into the matter. They have not cleared up the question altogether, but have come to certain conclusions, the most important of which are :—1. That there is a definite morbid entity associated with the presence of *Trypanosoma cruzi* in the peripheral blood in acute cases. 2. That in so-called chronic forms the parasite may not be found either in life or in the tissues after death, but that this fact does not disprove its presence, and that further, more minute search may discover it. 3. As regards special forms of chronic cases—the cardiac and myxoedematous in particular—in one case of the former in whose blood the trypanosome had been found during life the finding was not confirmed at the autopsy, and the condition of myocarditis was indistinguishable from a syphilitic process, though it is acknowledged that in Chagas's disease the Wassermann reaction is negative and antisyphilitic treatment is unavailing. The whole question of goitre, myxoedema, and corresponding forms of American trypanosomiasis needs reconsideration, the Commission deciding that the areas in which the diseases occurred in some instances coincided, but whether there is any actual causal relation between the trypanosome and the thyroid condition was not proven.

In the latter part of the report Dr. Chagas's reply is given *verbatim* and consists practically of an amplified statement of the points found in all modern text-books on tropical medicine relative to this disease. [The reviewer is of opinion that this article would have been of greater scientific value and would have added more to the dignity of the Society had the editor seen fit to expunge the personal and vituperative parts of the letters which passed between the protagonists.]

H. Harold Scott.

CHAGAS (Carlos). **Sobre a verificaçãe do "Trypanosoma cruzi" em macacos do Para,** (*Chrysothrix sciureus*). **Nota previa.** [*Trypanosoma cruzi* in Monkeys in Pará.]—*Sciencia Medica.* Rio de Janeiro. 1924. Feb. 29. Vol. 2. No. 2. pp. 75–76. With 1 plate.

——. **Infection naturelle des singes du Para** (*Chrysothrix sciureus, L.*), **par** *Trypanosoma cruzi.*—*C. R. Soc. Biol.* 1924. Apr. 4. Vol. 90. No. 12. pp. 873–876. With 4 text figs.

Whilst examining the blood of Para monkeys (*Chrysothrix sciureus*) parasites having the morphology of *Trypanosoma cruzi* were encountered. The infection was never intense in the monkeys, but young dogs proved very susceptible and died in a short time. Histo-pathological examination showed lesions similar to those found in man. Inoculation of guineapigs also succeeded, but the development of the infection was slower than in the dog.

In south Brazil the natural reservoir of the trypanosome is the Tatou (*Tatusia novemcincta*) and the intermediate host is *Triatoma geniculata*, and in north Brazil, where the human disease is as yet unknown, the parasite has been found in a monkey, but it is still to be determined whether the infection is pathogenic in monkeys and what is the intermediate host. The author considers that the parasite found

by him in Para monkeys is not identical with *T. prowazeki* described by Gonder and Berenberg-Gossler from the blood of *Brachiurus calvus* in the valley of the Amazon.

W. Y.

Blanchard (M.) & Laigret (J.). **Résultats éloignés du traitement de la maladie du sommeil par les fortes doses d'atoxyl. Traitement curatif et atoxylisation prophylactique.**— *Ann. Inst. Pasteur.* 1924. June. Vol. 38. No. 6. pp. 460–469. [3 refs.]

Treatment of human trypanosomiasis in the first stage has been profoundly modified at Brazzaville during the past few years by the employment of large doses of atoxyl instead of small or moderate doses. Atoxyl treatment in large doses takes two different forms: (1) at Brazzaville and in large centres the cure is prolonged for 6 weeks and has for its object a definite sterilization; (2) in the bush large numbers of patients are treated by 2 injections at 15 days' interval with the object of producing temporary sterilization of the blood and of so arresting the progress of the epidemic. The results obtained by these two methods are contrasted in the present paper.

Curative treatment. The treatment by massive doses of atoxyl practised at Brazzaville consists in giving 6 subcutaneous injections each of 1·5 to 2 cgm. per kilo of body weight. Actually the dose is almost always 2 cgm. per kilo and frequently exceeds this. The injections are given at 14 day intervals; generally the patient received 5 intravenous injections of emetic between the doses of atoxyl, but this had no effect on the result. In considering the results, only those are counted who received the above treatment only and again only those whose cerebro-spinal fluid contained less than 20 cells per cmm. and less than 0·2 gm. of albumen per litre. Of the 100 cases thus treated 6 relapsed during the first year. In the second year a certain number of cases progressed to the seeond stage of the disease; these formed 27 per cent. with 5 deaths; after three years 67 remained apparently in good health.

Prophylactic treatment. This method consists in administering two injections of atoxyl each of 1 to 1·2 gm. for an adult (about 2 cgm. per kilo of body weight) at an interval of 10 to 15 days, and if possible repeating it twice in a year. In the results given below only cases similar to those described above are considered. Of the 100 cases so treated 25 relapsed within a year; probably some were re-infections.

Table comparing the results of the prophylactic treatment and the therapeutic treatment.

I.—Prophylactic results.

	2 Atoxyl. per cent.	6 Atoxyl. per cent.
3 months after treatment:		
Relapses	6	1
Sterilizations	94	99
6 months after treatment:		
Relapses	17	3
Sterilizations	83	97
9 months after treatment:		
Relapses	20	6
Sterilizations	80	94
1 year after treatment:		
Relapses	24·5	6
Sterilizations	75·5	94

II.—Curative treatment.

After the first year results were :	2 Atoxyl. per cent.	6 Atoxyl. per cent.
Entered into second stage	6·5 ..	4
Relapsed without meningeal reaction	22·5 ..	6
Total of cases not cured	29 ..	10
Number apparently cured	71 ..	90

W. Y.

Sicé (A.). **Notes résumées sur l'évolution, le pronostic, le traitement de la trypanosomiase, chez les indigènes du Gabon.**—*Bull. Soc. Path. Exot.* 1924. Feb. 13. Vol. 17. No. 2. pp. 179–191. [9 refs.]

This paper records observations made in the treatment of 217 cases of sleeping sickness treated between 12th August 1919 and 31st December 1920, and followed up to December 1921. The author divides the cases into four groups :—The first consists of 36 patients all in early stages of the disease. Details are given concerning 7 of these cases which can be considered as types. The cases received from 2 to 6 gm. of atoxyl and ·4 to 1·0 gm. of emetic and all were in excellent health and apparently cured at the end of the observation period. The second group comprised 104 cases also recognised and treated in the early stages of the infection. Details are given of six of these cases ; all received several courses of atoxyl and emetic, and although all were in good state at the end of the observation period the prognosis is reserved. The third group consists of 41 cases concerning whom no information is available, and the last of 36 cases, all of whom died, notwithstanding energetic and prolonged treatment. These cases were in an advanced state when treated. Of the two types of cerebral cases described by Martin and Darré, viz., the diffuse forms characterized by a meningeal syndrome with a subacute course, and the circumscribed form, the former was most commonly met with by the author. In conclusion the author lays stress on the importance of proper nourishment in the treatment of the patients.

W. Y.

Low (George C.). **A Second Series of Cases of Human Trypanosomiasis treated by " Bayer 205." With an Account of the After-Histories of Some of the First Series.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1924. Feb. 21. Vol. 17. No. 8. pp. 464–473. With 2 charts. [1 ref.]

Further information is given regarding the nine cases of sleeping sickness treated by Low and Manson-Bahr with " Bayer 205 " [this *Bulletin*, Vol. 20, p. 323]. Six of the cases are well and have not received any further treatment, one relapsed and was treated with tryparsamide, and two are dead. Four further cases (*T. gambiense*) have been treated with the drug and details are given. The first of these had 12 injections of " Bayer 205 "—each of 1 gm.—between 7th April and 30th June 1923 ; the second 10 injections between 27th June and 30th August 1923 ; the third 10 injections between 7th August and 10th October 1924 ; and the fourth, who had already had 3 injections before reaching England and whose blood was then negative, was given 10 injections between 24th October and 28th December 1923. All did well, but all developed albuminuria.

W. Y.

WALRAVENS (P.). **La maladie du sommeil dans la région de la Luvua. Traitement par le "Bayer 205."**—*Ann. Soc. Belge de Méd. Trop.* Brussels. 1924. Jan. Vol. 3. No. 3. pp. 223–231.

The author was sent by the Congo Government to join KLEINE'S Commission in order to study the therapeutic action of "Bayer 205." The district chosen had been studied during 1911–1914 by LEJEUNE, who found that about 6 per cent. of 25,000 examined were infected with trypanosomiasis. LEJEUNE had commenced an active campaign against the disease, but it was interrupted by the War. The disease has far from disappeared in the region. A table is given showing the rate of infection found in the different groups of villages visited in the Luvua district and shows that of a total of 3,368 persons examined 336 had enlarged glands and trypanosomes were found in 92 (2·7 per cent.); this figure is, however, certainly below the actual figure, for reasons which are discussed.

Diagnosis was most frequently made by examination of fresh gland juice, but sometimes parasites were found only after several punctures. In certain very suspicious cases there were no glands and in these trypanosomes were often found by examination of thick blood films, a method for making which is described.

The author reached the following conclusions regarding the endemicity of human trypanosomiasis in the Kiambi region :—

(1) The disease raged always with intensity, causing an unequally high proportion of patients in the places visited.

(2) The symptoms were severe and the mortality is probably high, 3 of 73 patients observed dying within two months.

(3) A considerable proportion of children between 6 and 15 years of age were infected. The author's attention had been frequently drawn to the comparatively small number of children met with in certain villages: this he ascribes to trypanosomiasis.

The drug was given intraveneously, 3 injections in relatively early cases and 4 in advanced cases. Injections were given according to the following plan, 1 gm. being given to adults and ·5 gm. to children :—

1st day; first injection.
3rd day; second injection.
5th day; third injection in severe cases.
13th day; third injection in early cases.
15th day; fourth injection in severe cases.

The results of treatment have been especially apparent in advanced cases and it is remarkable how quickly they have improved physically, but in patients suffering from mental symptoms the improvement has been less noteworthy; of four demented cases exhibiting great excitation two have become calm but remain incoherent, one is slightly improved and the last is unchanged. Trypanosomes disappeared from the blood and gland juice in all cases, usually in less than 48 hours, and a month after cessation of treatment all were still negative. The author adds that it is of importance that these cases be followed up, as it is only after 6 to 12 months or more that we can talk of definite cures.

As illustrating the beneficial effects of the drug in patients in a late stage of the disease, the author quotes the case of a woman who could not walk without support and in whom the prognosis seemed hopeless.

A month after commencement of treatment the patient was able to walk alone, has gradually recovered her strength, and is now in a state of convalescence. She had trypanosomes in the gland juice and in the spinal fluid before commencement of treatment.

In another very advanced case, however, who had four injections of "Bayer 205," scanty trypanosomes were found in the spinal fluid 3 weeks after cessation of treatment. This is comparable with a number of observations made by KLEINE in Rhodesia. The author concludes that "Bayer 205" is a very active trypanocide, which cures in probably 80 to 90 per cent. of cases and which sterilizes the peripheral vascular and lymphatic system in a still larger proportion of cases. It is hence of great value as a prophylactic in the regions where the disease is raging.

In conclusion, the author remarks that patients after treatment with the drug generally suffered from albuminuria, which persisted for a more or less prolonged period, often more than six months. In animals which were killed by large doses of the drug, degenerative lesions were noted in the liver and kidneys.

W. Y.

FONTANA (Luc). **Résultats statistiques du traitement de la trypanose humaine par le Bayer 205.**—*Arch. Méd. Belges.* 1924. Apr. Vol. 77. No. 4. pp. 271–273.

The author gives later information of the cases treated by KLEINE at Kiambi in the Tanganyika-Moero district. Those which relapsed did so between the sixth and twelfth months, and the last six months of the year 1923 will in all probability give an estimate of the exact value of the drug. Of the 83 cases treated during the first six months of 1923, 65 were in the first stage of the disease and 18 in the second with altered cerebrospinal fluid. Of the former, 51 are probably cured, 8 have relapsed and 8 are dead. The author remarks that the average time for reappearance of trypanosomes in the blood after the last injection of Bayer 205 was 226 days and the minimum time 145 days. He concludes that if Bayer 205 has not fulfilled all the hopes raised, nevertheless it is a drug of great value in virtue of the long period of sterilization of the peripheral blood which it produces.

W. Y.

BLANCHARD & LEFROU (G.). **Essais du stovarsol dans la trypanosomiase humaine.**—*Bull. Soc. Path. Exot.* 1924. Mar. 12. Vol. 17. No. 3. pp. 214–216. [2 refs.]

The therapeutic action of stovarsol (acetyloxyaminophenyl arsenic acid) was tested on eight natives suffering from the first stage of trypanosomiasis, *i.e.*, with normal cerebrospinal fluid. It was found that in order to sterilize the circulation by a single oral administration it was necessary to give 2·5 to 3·0 gm. of the drug; this dose was well borne and did not give rise to any trouble. The sterilization thus obtained was of short duration. The repetition at 24 hour intervals of smaller doses gave no better results. The authors conclude that stovarsol is not likely to play much part in the treatment of sleeping sickness, but the results are interesting, as it is the first example of a drug administered by the mouth having a definite trypanocidal action.

They mention that 189 or oxyaminophenylarsenic acid, which acts well in experimental infections of mice and guineapigs when given orally in doses even as large as 9 gm., has no sterilizing action on human beings, whereas 190 or stovarsol, a drug which has only a very moderate trypanocidal action in the case of infected mice and guineapigs, exerts, on the contrary, a quite definite action when given orally to infected human beings.

W. Y.

Blanchard (M.) & Laigret (J.). **Sur quelques cas de guérison de la trypanosomiase humaine à la deuxième période.**—*Bull. Soc. Path. Exot.* 1924. May 14. Vol. 17. No. 5. pp. 368–372.

At the Loanda Congress one of the authors and Lefrou recorded briefly a case of sleeping sickness which at the time of treatment with large doses of novarsenobillon was in the second stage of the disease and which had been observed for more than five years, during the last three of which the patient had been perfectly well; repeated examinations of the blood were negative and the cerebrospinal fluid was absolutely normal. Since the Loanda Congress the authors have succeeded in obtaining at the Pasteur Institute of Brazzaville details of three other cases of a similar kind. Details of these four cases are given. The first case was a child of 12 years of age, recognised as infected in December 1918, and treated by small doses of atoxyl. In April 1920, 6 large injections of atoxyl were given, there was no relapse, but lumbar puncture made in January 1921 revealed trypanosomes in the spinal fluid. On 15th January she was given ·2 gm. of novarsenobenzol and this was followed by severe but transient symptoms of arsenical poisoning; 12 days later a second injection of ·15 gm. was given. Six months later blood and spinal fluid were negative and normal and they have remained so up to January 1924, the child having enjoyed perfect health. The other cases are of a similar nature, but were adults and were treated by atoxyl.

The next question which arises is whether cases in the second stage of the disease ever recover spontaneously. Details are given of a case which seems to bear on this point. The patient was recognised as infected in 1911 and diagnosed clinically as in the second stage of the disease on account of the following symptoms: Tremors, loss of equilibrium, oedema of the face, a very poor general condition; lumbar puncture was not permitted. Up to July 1911 he was given a course of treatment with the emetic of aniline. The blood was rendered negative, but the nervous symptoms increased and in February 1912 the patient was given a course of atoxyl in relatively large doses. At the end of 1912 there was a relapse and two injections of arsenobenzol were given; these caused sterilization of the blood, but no improvement in the meningeal condition. In April and October 1913 lumbar puncture showed trypanosomes in the spinal fluid. An attempt at intrathecal treatment with arsenobenzol was made. In June 1914 the patient was completely paralysed in the legs; he remained in hospital in the same state until 1922, when he disappeared. In January 1924 he turned up walking with the aid of two sticks and in excellent general health; lumbar puncture was refused. The authors state that it is certain that in this case the improvement could not have been due to any therapeutic influence.

The conclusion is that in exceptional cases human trypanosomiasis well advanced in the second stage evolves towards a state which can be regarded as equivalent to a complete cure.

W. Y.

Van den Branden (F.). **Durée de la guérison apparente chez quelques anciens trypanosomiés traités.**—*Ann. Soc. Belge de Méd. Trop.* Brussels. 1924. Jan. Vol. 3. No. 3. pp. 359–363.

During the author's last sojourn at Stanley-Pool, he has had occasion to re-examine a number of old cases of sleeping sickness treated by Broden, Rodhain, Dubois, Mouchet and himself. The population of Leopoldville and Kinshara is an agglomeration of all the races of the Congo and is in a state of constant flux ; hence it is difficult to follow cases for many years. This explains the comparatively small number of cases followed over prolonged periods. All the patients had normal spinal fluid and were in the first stage of the disease at the commencement of treatment. Details are given regarding 18 of these old standing cases, which are apparently cured after an average of 9 years and 9 months after cessation of treatment.

W. Y.

Morgenroth (J.) & Freund (R.). **Ueber die Wirkungsweise von "Bayer 205" bei der experimentellen Trypanosomeninfektion der Maus.** [The Mode of Action of "Bayer 205" in Experimental Trypanosomiasis of the Mouse.]—*Klin. Woch.* 1924. Jan. 8. Vol. 3. No. 2. pp. 53–55. [7 refs.]

Reference is made to the observations of Mayer and Zeiss on the difficulty of obtaining in the mouse a strain of trypanosomes resistant to "Bayer 205" [this *Bulletin*, Vol. 17, p. 334] and also to the fact that Kleine and Fischer readily obtained "Bayer 205" fast strains of *T. brucei* in monkeys and in cattle [*loc. cit.*, Vol. 21, p. 56]. Freund succeeded, after prolonged experiments, in obtaining in mice a highly and persistently "Bayer 205" resistant strain of nagana (strain Prowazek) and it is remarked that this strain was also resistant to trypanblue.

Morgenroth and Freund could not repeat Mayer and Zeiss's method of treatment and relapse, as with the nagana strain used by them relapses never occurred after treatment with "Bayer 205," although they were observed in the use of other drugs. Cure was obtained by subcutaneous injection of ·5 cc. of 1 : 10,000 solution of the drug per 20 gms. of body weight in mice, trypanosomes disappearing after a day or two and never reappearing ; even ·17 cc. of the above solution sometimes caused a disappearance of trypanosomes and in one case there was no relapse. From these observations the authors conclude that not only has "Bayer 205" a trypanocidal action, but also that it is capable of influencing the growth of relapsing strains. In order further to investigate the subject, it was necessary to eliminate the trypanocidal action of the drug and to allow that part of the work to be done by another drug. The drug chosen for this purpose was tartar emetic, the primary trypanocidal action of which was regularly followed by a relapse.

Mice were injected subcutaneously with ·3 cc. of diluted mouse blood containing 1 to 2 trypanosomes per microscopic field and at the same time ·5 cc. of a 1 : 20,000 solution of " Bayer 205 " per 20 gms. of body weight was injected intraperitoneally. Some of the mice did not receive the drug and served as controls. Details of one of many similar experiments are given in a table. All the mice became infected, and when the infection was sufficiently advanced all the animals were given ·3 cc. of 1 : 1,000 solution of tartar emetic per 20 gms. of body weight. The mice which previously received the " Bayer 205 " did not relapse after the tartar emetic, whereas controls did. In further experiments it was found that when the dose of " Bayer 205 " was reduced to ·5 cc. of a 1 : 40,000 per 20 gm. of body weight, relapses occurred. These experiments show that although " Bayer 205 " in the doses given exerts little or no prophylactic power over the infection, it nevertheless influences to a considerable extent the ultimate effect of the tartar emetic, which is qualitatively changed, inasmuch as the otherwise invariable relapses do not occur. The treatment of trypanosome infections with exceedingly small doses of " Bayer 205 " influences in a quite specific manner one of the functions of the trypanosome cell, viz., its power to become serum resistant, this function being crippled.

Reference is made to previous work of Morgenroth and Rosenthal,* who showed that a tantalum compound, although it did not influence the course of the infection, nevertheless caused the blood of the infected animal when injected into a susceptible one to be non-infective. Morgenroth and Freund also proved that the above-mentioned " Bayer " resistant strain was also resistant to this secondary action of the drug, as it relapsed after treatment with tartar emetic.

This work, the authors consider, emphasizes the importance of combined therapy in the treatment of trypanosomiasis.

W. Y.

Kritschewsky (J. L.) & Brussin (A. M.). **Von der Wirkung hypertoxischer Dosen Salvarsan auf salvarsanfeste Trypanosomenrassen in Verbindung mit der Frage von der Pathogenese der Schlafkrankheit und der Parasyphilis.**—[On the Effects of Hypertoxic Doses of Salvarsan on Salvarsan-fast Trypanosome Strains in relation to the Pathogeny of Sleeping Sickness and Parasyphilis.]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* I Teil. Orig. 1924. June 2. Vol. 39. No. 6. pp. 513–549. [22 refs.]

The authors have found that if salvarsan is injected subcutaneously in acid solution doses are tolerated 3–6 times as great as those in alkaline solution.

The following summary is given :—

1. The organotropy of salvarsan to the skin and subcutaneous tissue and the possibility, demonstrated by us, of a simultaneous organotropy and parasitotropy have shown us the means of introducing into an organism doses of salvarsan which are several times as large as the doses hitherto employed.

2. It was clear that the possibility of " hypertoxic " doses would be of great importance in therapeutics. An attempt was therefore made to sterilize a salvarsan-fast organism.

* Summarized at some length in *Sleeping Sickness Bulletin*, Vol. 3, pp. 115 & 301.

3. The possibility has been demonstrated of destroying salvarsan-fast trypanosome strains in the same organism in which they acquired their resistance.

4. After a treatment with "hypertoxic" doses 12·5 per cent. of the mice infected with salvarsan-fast trypanosomes had been sterilized (carefully controlled).

5. In animals, in which the salvarsan-fast strains could not be completely destroyed, "hypertoxic" doses showed the following results: In 99·12 per cent. a remission occurred (in animals treated with an alkaline salvarsan solution only 59·2 per cent.); in the majority of cases this remission occurred within 24 hours (70·3 per cent.), 28·5 per cent. on the second day and 12 per cent. after 48 hours. In animals treated with the alkaline solution the remission hardly ever lasted more than 8 days, in those treated with "hypertoxic" doses an 8-day remission was a rarity; it usually lasted much longer, often as long as 2 months.

6. Mice from the organism of which salvarsan-fast trypanosome races do not disappear after one treatment with "hypertoxic" doses can be sterilized by a second treatment, or else their remission period lengthened.

7. A hypothesis is suggested to explain the lack of success in the treatment of sleeping sickness by drugs, and for the appearance of parasyphilis, as the result of a formation in the human body of drug-fast trypanosomes and spirochaetes.

8. Observations were made on the customary doses of salvarsan and on the possibility of increasing them.

W. Y.

MIGNOLI (Alfonso). **Del comportamento della tripanocidiasi in diverse forme morbose.**—*Riforma Med.* 1924. June 23. Vol. 40. No. 25. pp. 577–579. [13 refs.]

LAVERAN and MESNIL noted the trypanocidal action of human serum on *T. brucei*, and further, that, though the maternal serum possessed this power, that of a new-born child had none. Following this up the author tried the trypanocidal effects of human sera in various diseases. Apparently the property is peculiar to human serum, that even of anthropoid apes being inert; he does not agree that it is attributable to the leucocytes, since it was not diminished by the existence of a leucopenia; also that it is not due to complement action because inactivation of the serum did not affect the result. He is of opinion that it is hepatic in origin and is diminished when the function of the liver is disorganized. He inoculated a large number of rats with *T brucei*. All showed infection within 48 hours and controls died in 2–3 days. To the others was given 0·2 cc. serum for every 20 gm. of body weight. Sera were tried from 25 patients, among whose maladies were tuberculosis in various stages, carcinoma of the head of the pancreas with marked jaundice, pancreatic diabetes, catarrhal jaundice, bronchopneumonia, enteric fever, encephalitis lethargica, cardiac valvular affections, and so on. He found that serum from a case of advanced tuberculosis was less trypanocidal than that from an early or improving case, that the presence of malignant disease did not affect the trypanocidal action, but that liver conditions altered it in the degree to which the liver cells were injured by disease.

H. Harold Scott.

Lloyd (Ll.) & Johnson (W. B.). **The Trypanosome Infections of Tsetse-Flies in Northern Nigeria and a New Method of Estimation.**—*Bull. Entom. Res.* 1924. Mar. Vol. 14. Pt. 3. pp. 265–288. With 3 plates & 6 text figs. [15 refs.]

The authors point out that in studying the relationship of tsetse flies to the wild fauna a rapid method of estimating the trypanosome infections of the flies is of great utility. Between September 1921 and April 1922, 2,500 tsetses comprising 448 *G. morsitans*, 1,497 *G. tachinoides* and 534 *G. palpalis* were dissected and fully examined, all the organs containing flagellates being permanently mounted. The slowness of this method is its chief drawback, as not more than 40 flies could be dealt with in one day. The first attempt at a more rapid method of examination was made by collecting from each fly before dissection the small drop of salivary exudate which can be expressed from the tip of the proboscis by slightly squeezing the insect. The numbers of mature infections (infective forms) of the *T. vivax* and *T. congolense* groups discovered by dissection were :—in *G. morsitans* 44, in *G. tachinoides* 33 and in *G. palpalis* 9, whereas the number which could have been discovered if the salivary exudate only had been examined were 22, 10 and 9, respectively.

Since all infections of the *vivax* group and all mature infections of the *congolense* group are discoverable by examination of the proboscis alone a series of examinations of this organ was next carried out, and 3,458 *G. tachinoides* and 623 *G. morsitans* were thus examined in the last eight months of 1922, a few hours each week being devoted to the work. The objection to the method is that it does not reveal the mature infections of the *brucei* group, though some are found by it.

With regard to the development of *T. gambiense* in *G. palpalis*, the authors quote from Miss Robertson as follows :—

" The [salivary] gland [of the tsetse-fly], as is well known, is composed of (1) a narrow tubular part, which leads back to (2) a slightly broader cellular part, which in turn leads to (3) the glandular part where the full width of the organ is attained. The trypanosomes settle down and attach themselves in the second part of the gland or at the entrance to the third part, the rest of the gland being quite free from trypanosomes."

They add that later, of course, the whole gland is involved. In order to detect mature infections of the *brucei* group a method of dissection was evolved which yields the first two parts of the salivary glands. The rarity, however, with which trypanosomes were encountered makes the authors doubt whether none were missed. Of the seven mature infections of the group, viz., two *T. gambiense* and five *T. brucei* obtained in laboratory infected *G. tachinoides*, it was the authors' opinion that five could not have been missed by the rapid method of dissection, whereas two could not be detected in the fresh preparation of the whole gland, although trypanosomes were subsequently found in stained films.

By the above rapid method flies can be dealt with at an average rate of 50 or more an hour. All mature infections of the *vivax* and *congolense* groups and most infections of the *brucei-gambiense* group are discovered.

A description is given of the technique employed in the making of (1) The full dissection ; (2) Proboscis dissections, and (3) Proboscis

and salivary gland dissections; the procedure is well illustrated by six diagrams.

Identifications of infections.—The trypanosomes discovered were referred to their groups by a combined study of developmental and infective forms, while the position in the fly is an additional aid. Four species of pathogenic tsetse-borne trypanosomes occur in Nigeria, viz., *T. gambiense*, *T. brucei* (*T. pecaudi*), *T. congolense* and *T. vivax*. All four species were transmitted by the authors in the laboratory. *T. simiae* is not known to occur in West Africa nor has *T. rhodesiense* been recorded there.

T. vivax group.—The developmental forms in the labial cavity are all free-flagellated crithidia in compact fixed colonies; they are rarely truncated at the posterior end (compare *T. congolense* group). The pre-infective forms are crithidia with the blepharoplast and nucleus close together at the anterior end; they are free-flagellated and somewhat undulant. These forms invade the hypopharynx, and after an anterior movement of the nucleus become infective forms, which are slender, markedly undulant, free-flagellated, with a sharply pointed anterior end, and, in general, closely resembling the blood forms except for size, the average length being 14·4 to 14·9μ.

T. congolense group.—The site of development is the mid-gut, where only trypanosomal forms occur. The shorter forms are aflagellate. A longer free-flagellate form is produced which moves forward to the proventriculus and thence to the labial cavity. These forms are indistinguishable from the corresponding forms found in the *brucei-gambiense* group. In the labial cavity the organisms become aflagellate, or almost aflagellate crithidia, which are found in loose colonies. The individual crithidia are very frequently truncated at the posterior end. The only form in the proboscis which can be confused with *T. vivax* is a very slender free-flagellated form with the blepharoplast in close contact with the nucleus at the posterior end. This is probably in the pre-infective stage, as it was seen to invade the hypopharynx. The infective forms which are produced in great profusion are small, stumpy, aflagellate organisms with a blunt posterior end, feebly undulant, and closely resembling the smaller forms of *T. congolense* as seen in the blood; the average length is 11·1 to 11·2μ.

T. brucei-gambiense group.—The first phase of development occurs in the mid-gut, and the infection in this site can be distinguished from the *T. congolense* group by the fact that while the organisms of the latter species are almost aflagellate, those of *T. brucei* and *T. gambiense* are almost always free-flagellated. The completion of the gut development occurs when the proventriculus is invaded by long, slender, free-flagellated forms, indistinguishable from the comparable stage of *T. congolense*. Slender forms invade the salivary glands by way of the labial cavity and hypopharynx and become converted in the glands into short, broad, free-flagellated crithidia, which could not be distinguished from corresponding forms of *T. vivax*, except by the position in the fly. The infective forms have a blunt, posterior end and a more uniform width than those of *vivax* and the free flagellum is shorter. Transitional forms between the crithidia and the infective stage are common.

T. grayi.—This species is only recorded in the gut of the fly. It is at once distinguished from the foregoing species by the invariable presence of broad crithidial forms.

An analysis of the infections discovered by full dissection of the flies is given in a table.

The Trypanosome Infections found by Complete Dissection of Tsetse-flies in various Localities in N. Nigeria. All in Percentages.

Fly.		*G. morsitans.*	*G. tachinoides.*		*G. palpalis.*
			Wild ungulata common.	Wild ungulata very scarce.	
Number examined		448	1,093	404	534
T. vivax group	Mature ..	6·5	2·0	0·7	1·5
	Immature	12·3	5·6	1·0	1·1
	Total ..	18·8	7·6	1·7	2·6
T. congolense group	Mature ..	3·1	0·6	0·5	0·2
	Immature	5·1	1·3	0	0·4
	Total ..	8·2	1·9	0·5	0·6
T. brucei-gambiense group.	Mature ..	0	0	0	0
	Immature	0·4	0·2	0	0
	Total ..	0·4	0·2	0	0

The authors state that it was never possible to compare the three prevalent species of tsetse in any considerable numbers from the same locality; strict comparisons between *G. morsitans* and *G. tachinoides* were made several times and the results are given. A section is devoted to the prevalence of *T. grayi* in *G. tachinoides* and *G. palpalis*; and the seasonal variation in infection, and comparison of infections in various areas, based on proboscis examination are discussed at some length.

The following summary and conclusions are given :—

"This paper has been written to describe a new method of rapid estimation of trypanosome infection in tsetse-flies and to show the possibility of obtaining important information by it rather than as a record of any knowledge which has been gained while it was being developed. By means of a dissection which yields the proboscis fully displayed and the important parts of the salivary glands in one preparation, all mature infections of the *vivax* and *congolense* groups of trypanosomes may be discovered and most of the *brucei-gambiense* group. It gives no information as to the pathogenicity of the parasites and does not serve to distinguish between such morphologically similar species as *T. brucei* and *T. gambiense*. These are great drawbacks, which can only be overcome by the use of elaborate fly-feeding experiments. Compared with these latter, however, it is a much less cumbersome method, and in the main as rapid, while it yields, within its limits, more accurate statistics. By these it is possible to study the infection in the fly in relation to animals with which it is in contact and in various ways light is thrown on the bionomics of the insect.

"The method is sufficiently sensitive to record at once the effect of any change in local conditions. An instance of this occurred at Mashiwashi, when the disturbance in a patch of dense forest due to building and a certain amount of fly-catching reduced the proboscis infection in one part from 18·3 to 4·1 per cent. within six weeks, to be followed by a corresponding rise after the disturbance ceased.

"There is an indication that in at least one of the pathogenic trypanosomes (*T. vivax*) an important seasonal variation in the proportion of infective flies (*G. tachinoides*) occurs, the mature infections increasing as the rains progress.

"Variations in the infections of *G. tachinoides* and *G. morsitans* in different parts of a very small area have been found by the proboscis examination. To have discovered this so fully by means other than quick

dissection would have entailed carrying out a series of fly-feeding experiments from each of ten foci in the case of *G. tachinoides*, and from each of three fixed spots in the case of *G. morsitans*—an impracticable undertaking.

"A comparison of the infectivity of the three prevalent species of tsetse for the country generally is given. *G. morsitans* is much more heavily infected with the main cattle-inhibiting trypanosomes (*T. vivax* and *T. congolense*) than is *G. palpalis* or *tachinoides*.

"It is also shown that the infection in *tachinoides* is heavier in spots where the wild ungulates are prevalent than in places where they are scarce. Where *G. morsitans* and *tachinoides* range together the infection in the former is double, or more than double, that in the latter. This is probably because *G. tachinoides* has no special predilection for ungulates as hosts.

"Some notes on the non-pathogenic *T. grayi* are included, with evidence that it is reptilian in origin."

In an appendix details are given of certain transmission experiments with *G. tachinoides* of *T. vivax*, *T. congolense*, *T. gambiense* and *T. brucei*.

W. Y.

Kleine (F. K.). **On a Recent Expedition to Africa to investigate the Action of "Bayer 205" in Trypanosomiasis.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1924. Feb. 21. Vol. 17. No. 8. pp. 445–452. (Discussion pp. 452–463).

——. **Ueber meine Reise nach Afrika zur Prüfung von Bayer 205.** [On my Expedition to Africa to test the Action of Bayer 205.]—*Med. Klin.* 1924. Mar. 23. Vol. 20. No. 12. (1006.) pp. 367–369.

These papers are substantially the same as the one previously published and already noticed here [this *Bulletin*, Vol. 21, p. 56].

W. Y.

Bulletin de la Société de Pathologie Exotique. 1924. Apr. 9. Vol. 17. No. 4. pp. 288–290. [1 ref.]—**Prophylaxie de la maladie du sommeil.**

REVIEWS AND NOTICES.

BRITISH MUSEUM (Natural History). **Guide to the Mollusca exhibited in the Zoological Department, British Museum (Natural History).**—55 pp. With 47 figs. 1923. London: Printed by order of the Trustees of the British Museum. [Price 1s.]

Since pond-snails are the intermediary hosts by which the digenetic Trematodes are nurtured and disseminated, most medical men, in the tropics at any rate, want to know something about Mollusca; and in this well-illustrated "Guide" to the well-arranged and very complete collection of Mollusca exhibited in the galleries of the British Museum of Natural History they will find a large amount of useful information succinctly stated.

A. Alcock.

ROCKEFELLER FOUNDATION. **A Review for 1923. By George E. Vincent (President).**—48 pp. With 20 figs. & 1 map. 1924. New York.

"During the year 1923 the International Health Board, the China Medical Board, and the Division of Medical Education of the Rockefeller Foundation (1) supplied fellowship funds for 636 individuals in 29 different countries; (2) supported through the League of Nations interchange institutes for 54 public health officers from 27 nations; (3) arranged international visits of one commission and of 24 visiting professors; (4) furnished emergency relief in the form of medical literature or laboratory equipment and supplies to institutions in 15 European countries; (5) sent scientific material to Japan after the earthquake and invited a group of Japanese medical scientists to use the laboratories of the Peking Union Medical College as guests of the institution; (6) continued to contribute to schools or institutes of hygiene at Harvard, London, Prague, Warsaw, and São Paulo, Brazil; (7) co-operated in nurse training at Yale University and in France, Belgium, Brazil, China, and the Philippines; (8) accepted an invitation from Brazil to participate in a comprehensive attack upon yellow fever; (9) had a share in demonstrations of malaria control in 12 American States and conducted malaria surveys or studies in the United States, Brazil, Australia, Nicaragua, Porto Rico, Salvador, the Philippine Islands, and Palestine; (10) either continued or began antihookworm work in conjunction with 20 governments in various parts of the world; (11) contributed to 183 county health organizations in the United States, New Brunswick (Canada), and Brazil; (12) continued a study of the medical schools of the world by visits to Belgium, Austria, Czecho-Slovakia, Germany, Hungary, Poland, Turkey, Hongkong, the Straits Settlements, Siam, Canada, England, Scotland, Wales, the Netherlands, Mexico, and Colombia; (13) offered to contribute £280,750 sterling to the development of medical education in certain universities in the British Isles; (14) gave $500,000 to the University of Alberta, and pledged $250,000 to the University of Pennsylvania toward buildings for anatomy and physiological chemistry; (15) continued to support a modern medical school and teaching hospital in Peking; (16) aided two other medical schools and 25 hospitals in China; (17) assisted premedical education in several institutions in China and agreed to do this also in Bangkok, Siam; (18) lent representatives to governments and institutions for various types of counsel and service; (19) continued to support a disease reporting service of the Health Section of the League of Nations; (20) contributed to mental hygiene projects, demonstrations in dispensary administration, organization of dispensary work in France, and to other undertakings in the fields of public health and medical education."

A. Alcock.